The American Journal of Surgery

EDITED BY THURSTON SCOTT WELTON, M.D.

December 1942

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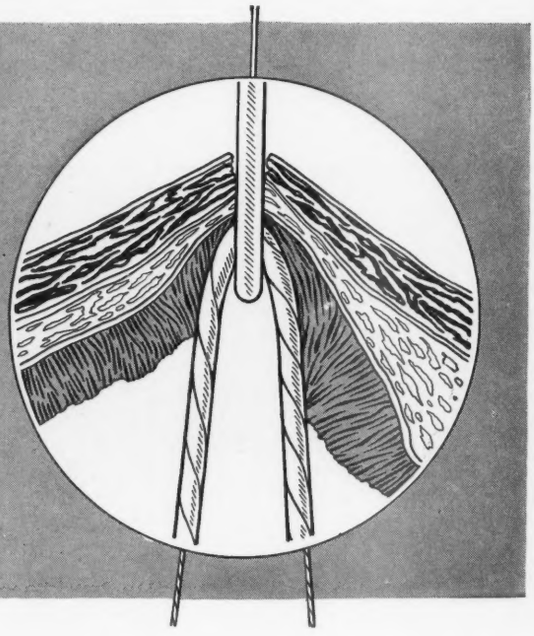

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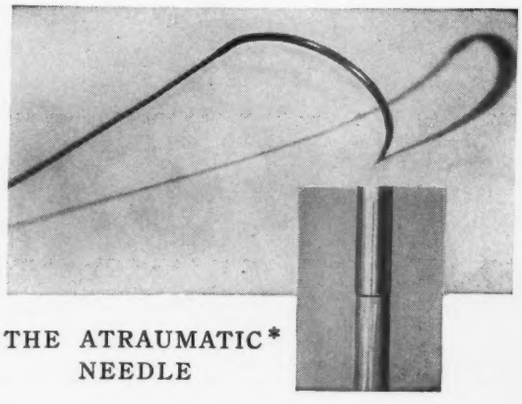

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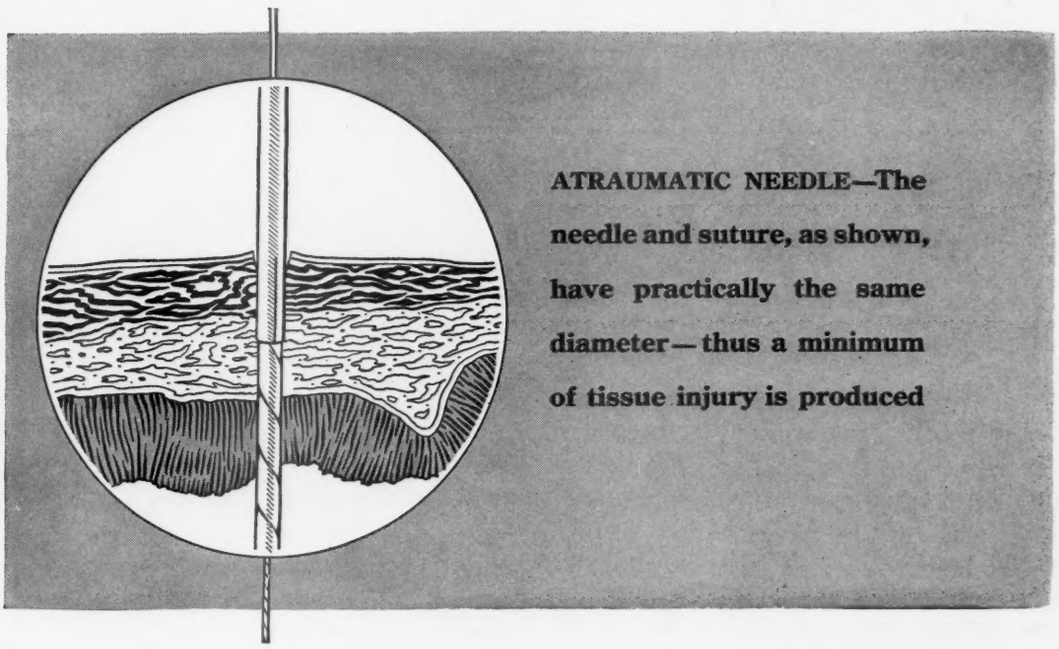

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In some individuals the fat layer may be several inches thick, permitting the formation of dead space, while in others it may be entirely absent, allowing the skin edges to roll under.

Within fat there is a thin layer of subcutaneous connective tissue which should be sutured whenever possible. Its repair provides extra strength for the wound and aids in maintaining hemostasis. This layer is usually hidden in the fat where it can only be located by means of forceps. It lies immediately subjacent to the skin when the subcutaneous fat is absent.

In general, two plans have been adopted to obliterate dead space without damaging the fat. Either tension sutures are employed or the subcutaneous connective tissue layer is approximated with very fine sutures.

The former plan is usually employed when the subcutaneous fat is very thick. When the subcutaneous fat is meager in amount, the connective tissue layer may be included in the bite of the skin suture. In all other circumstances separate suturing of the connective tissue layer is usually employed.

If the buried suture causes damage to fat, exudation and induration take place during the healing process. Sizes larger than No. 00 cause these changes plus tenderness and a discharge of clear fluid from the wound on the seventh to the tenth day of healing. The frequency of this complication with the larger sizes of buried sutures undoubtedly is the reason why some prefer to use tension sutures instead. However, when sizes No. 0000 or No. 00000 are employed as interrupted buried sutures in the subcutaneous fat, excellent healing is obtained. These sizes cause only minimal damage to the fat, yet they satisfactorily obliterate dead space and provide additional strength for the wound.

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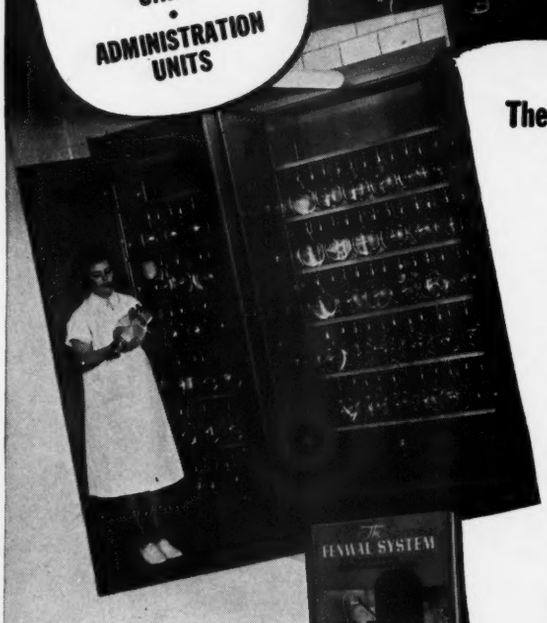

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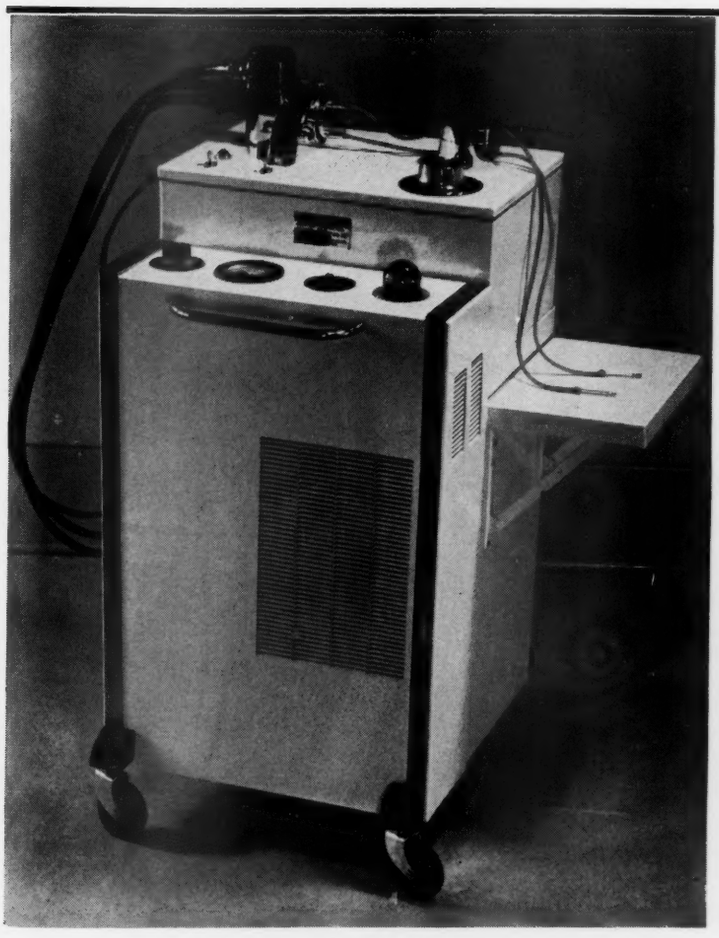

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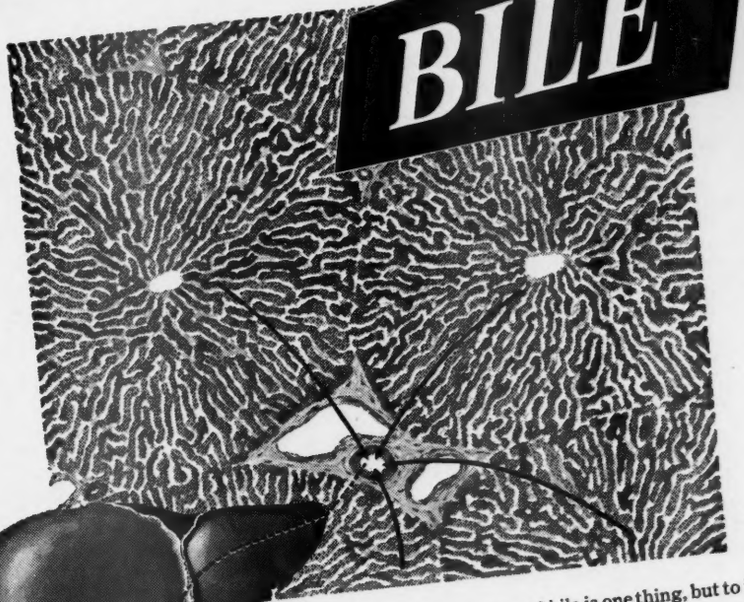

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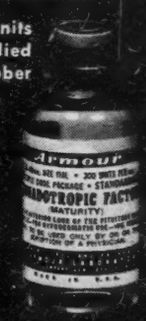

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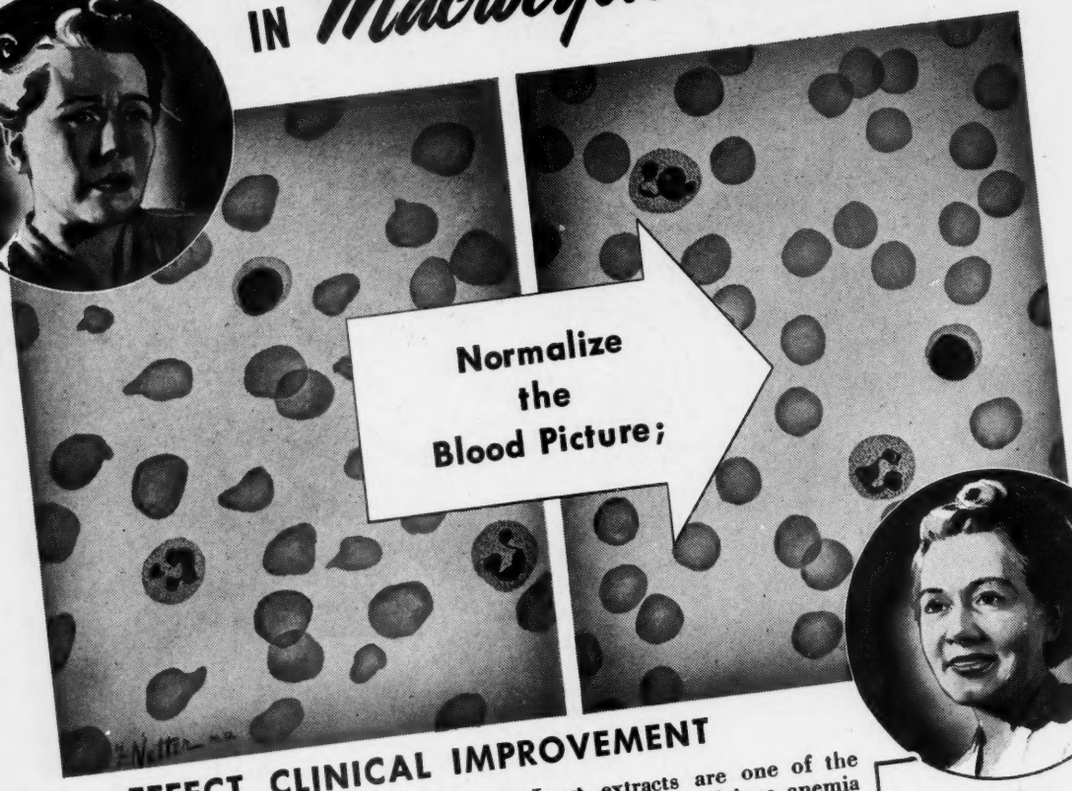

EFFECT CLINICAL IMPROVEMENT

NORMAL maturation of red cells within the body, according to Castle, is carried to completion only in the presence of adequate quantities of the hemopoietic principle. Absence or deficiency of this principle for any reason results in the development of a macrocytic anemia as in pernicious anemia, anemia of sprue, and one type of pregnancy anemia.

Liver therapy in the macrocytic anemias is thus largely a replacement measure—a replacement of the deficient hemopoietic principle. Adequate liver therapy tends to correct the macrocytosis —and as the blood picture improves, clinical condition is bettered.

The therapeutic benefits from liver therapy depend very largely upon the physiologic activity of the extracts employed. Inert extracts are one of the causes of failure in pernicious anemia therapy.

For this reason, in the manufacture of Armour liver preparations every precaution is taken to preserve the blood regenerating propensities of the fresh liver. Only the livers of young, actively growing animals are used and these are selected with great care. Every step in the processing is carefully checked and supervised and the finished product is accurately standardized. These methods are possible to the Armour Laboratories because of their tremendous supply of raw material, their almost unlimited resources and their staff of experts.

It is sound practice to specify "*Armour*" liver preparations.

Armour parenteral and oral liver preparations are standardized on pernicious anemia patients in relapse.

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4, 10 AND 15 U.S.P. INJECTABLE UNITS PER CC.

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A readily assimilable and therapeutically effective preparation for use when the oral route is preferred or for maintenance therapy.

3 tablespoons equal 1 oral unit, (45 cc.)

The Armour Laboratories have for many years pioneered in the development and preparation of medicinals of animal origin.

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CHICAGO, ILLINOIS

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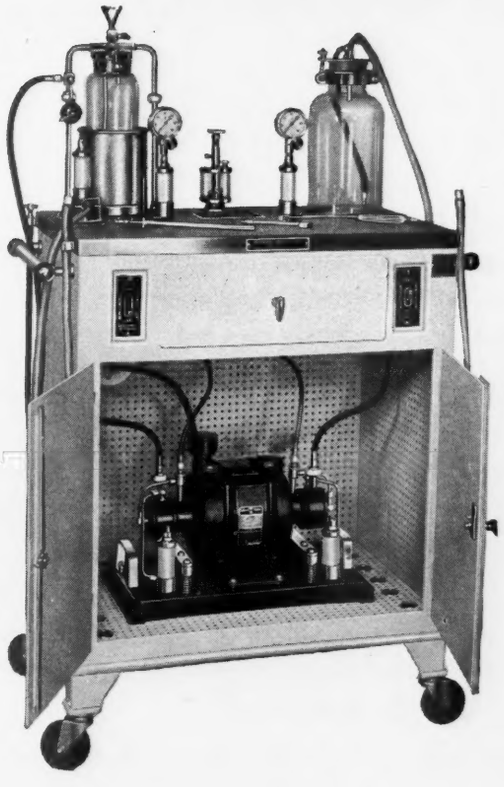

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Gretchen Guernsey, M.D., Paul Rannie, M.D.
Dept. Anesthesia, University of Kansas Hospitals
Pentothal Sodium in Relation to Ophthalmologic Procedures
Anesthesia and Analgesia, Vol. 20, No. 5, p. 277-281, Sept.-Oct., 1941

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*Veal, J. R., and Klepser, R. G., "Local Sulfanilamide Therapy in Surgical Infections"; Surgery. 10:947 (Dec.) 1941.

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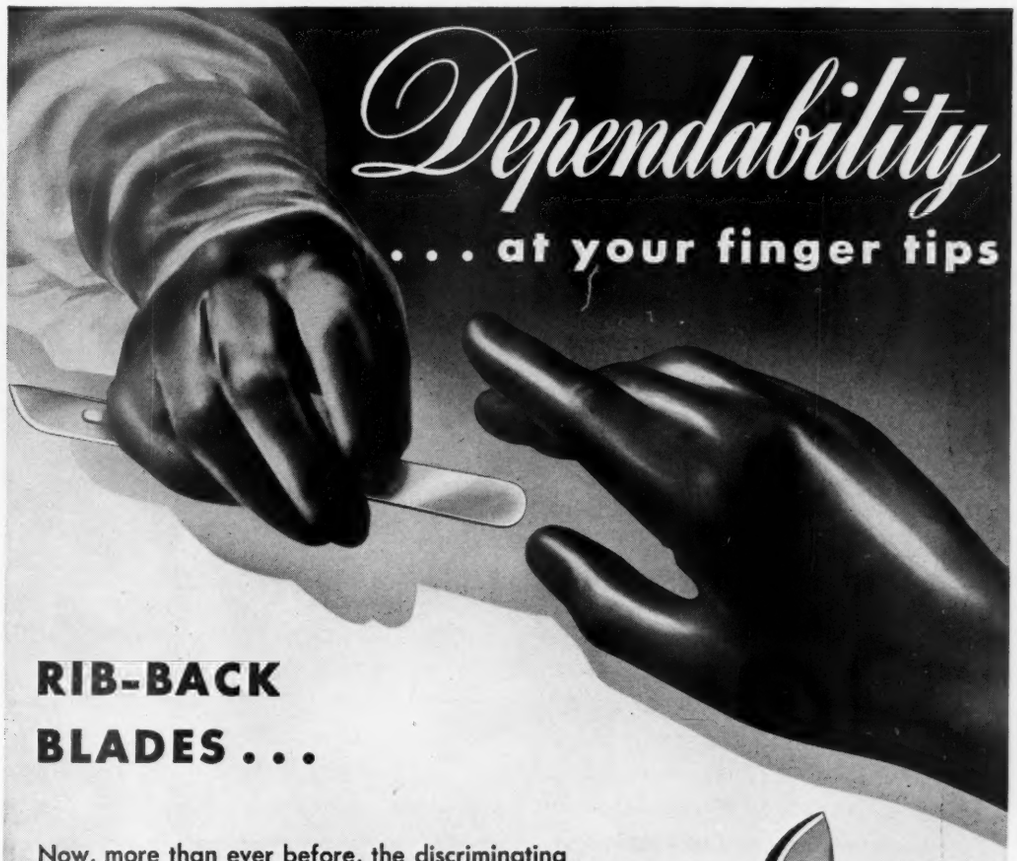

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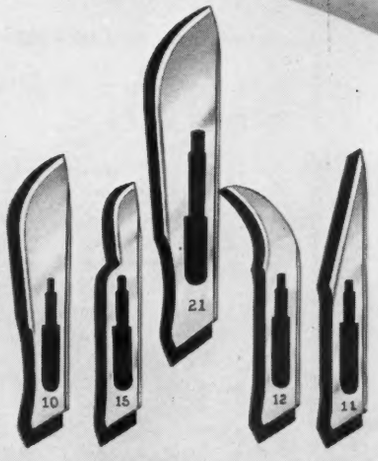

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5. Non-mercurial II, tincture	1:13,000	1:40,000
6. Non-mercurial II, solution	1:7,000	1:30,000
7. Mercurial I, tincture	1:4,000	1:26,000
8. Iodine, tincture	1:2,000	1:20,000
9. Iodine, aqueous	1:1,000	1:18,000
10. Mercurial II	1:3,000	1:10,000
11. Mercurial III	1:1,500	1:10,000
12. Non-mercurial III	1:3,000	1:8,000
13. Mercurial IV, solution	1:1,500	1:8,000
14. Mercurial IV, tincture	1:2,000	1:5,000
15. Mercurial V, tincture	1:2,000	1:3,000
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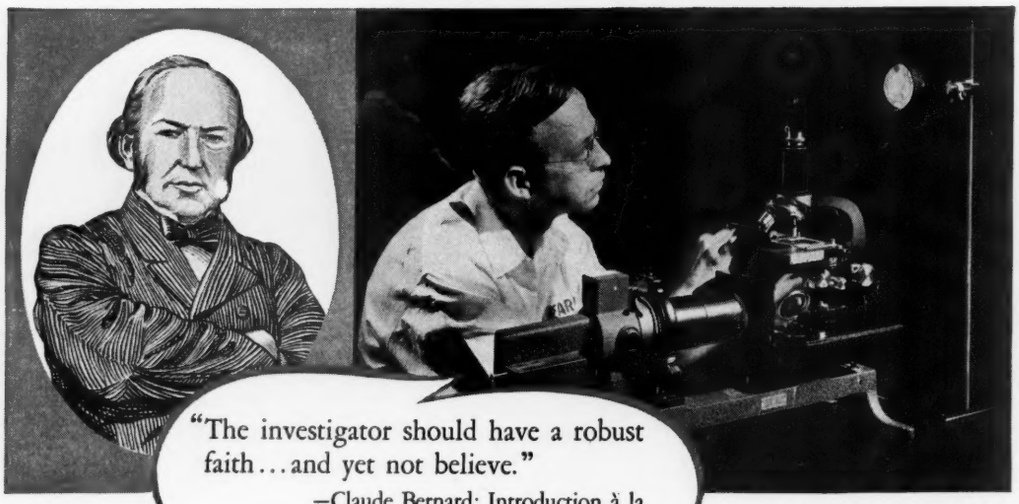

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—Claude Bernard: Introduction à la medécine expérimentale, 1865

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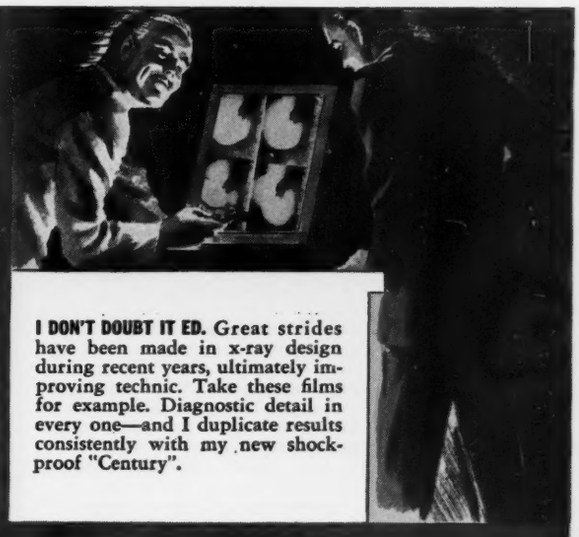

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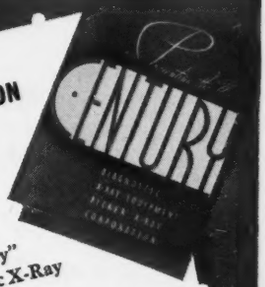

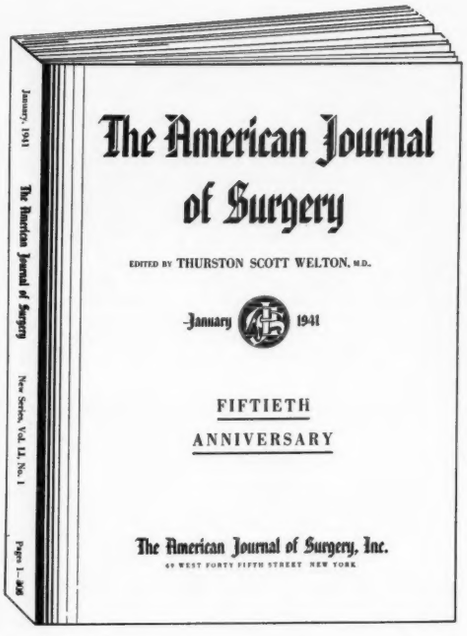
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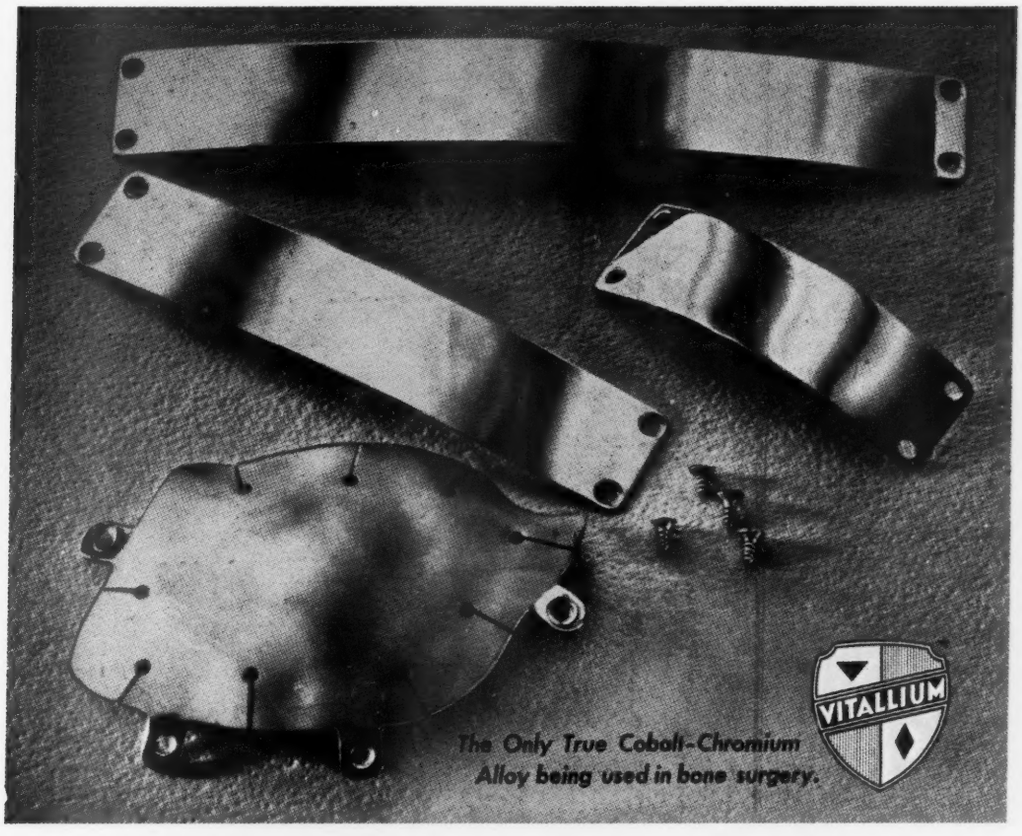

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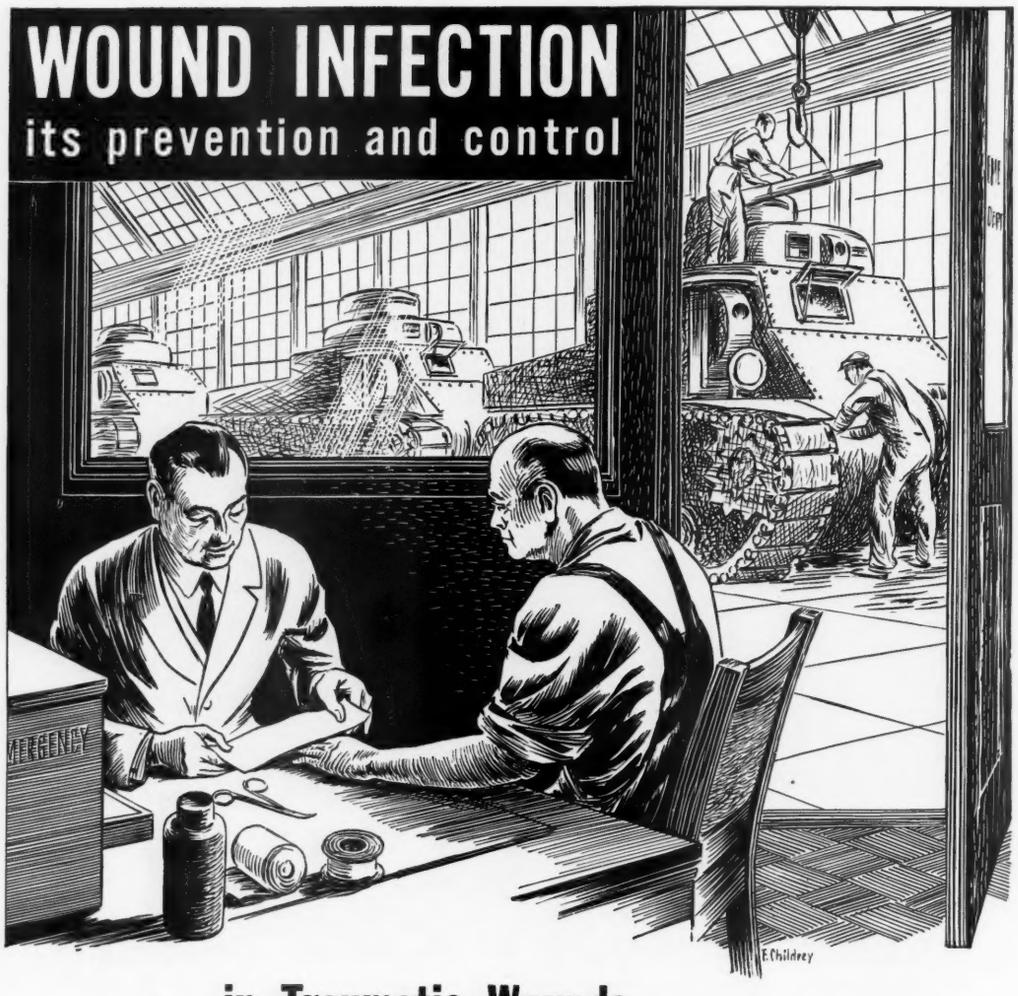

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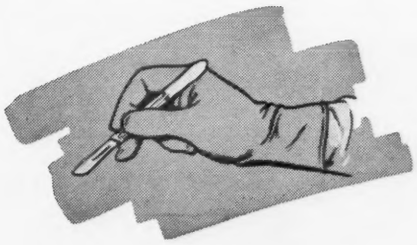

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A PRACTICAL JOURNAL BUILT ON MERIT

NEW SERIES VOL. LVIII DECEMBER, 1942 NUMBER THREE

Editorial

ESTABLISHMENT OF CARTILAGE DEPOTS FOR MILITARY AND CIVILIAN USE

RESERVES! Reserves! This seems to be the byword of our present day existence. Whether they are for defense, offense, or our own consumption, whether animate or inanimate, properly prepared, adequate reserves when soundly applied to the fullest capacity, will be the eventual positive answer to the successful culmination of the fight for "our way of life."

With the above thoughts in mind and knowing full well there will be considerable call in the future, I would like at this time to outline a simple but effective plan for the mass conservation of cartilage for either the immediate or subsequent use as cartilage grafts for reconstruction surgery.

The plan would be the establishment of cartilage depots in all military or civilian hospitals under proper supervision, where this type of graft would be used in its many phases of plastic and reconstructive surgery.

Since my original work ten years ago on what I called "Refrigerated Cartilage Isografts," numerous reconstructive surgeons throughout the country have successfully employed preserved cartilage grafts in dealing with their many reconstructive problems. From my own experience and from personal communications from other reconstructive surgeons, the use of preserved rib cartilage grafts in surgery as a permanent contour builder, supporter, and defect filler is now a scientifically proved fact.

The cartilage is obtained from human material preferably between the ages of eighteen and forty-five. The glistening white cartilage obtained from muscular individuals between the ages of eighteen and thirty is the ideal material. This cartilage is larger, heavier, preserves better, curls less, and is more suitable for sculpturing. With the wealth of available cartilage in the human body, one may be very select as to the donor. I use cartilage from individuals in the proper age group, who have met sudden death through some accidental means, excepting, of course, poison deaths. A Wassermann is done on the heart blood to prevent any medicolegal complications. Individuals who have, as their cause of death, tuberculosis, lues, septicemias, or other acute or chronic transmittable diseases, should not be used for donor subjects. One can readily see that, with the large number of accidental and functional deaths, a continuous and practically inexhaustible cartilage supply is available.

The cartilage isografts may be used interchangeably, regardless of race, sex, color, age (within certain limits) or blood grouping. The types of cartilage used to date have been septal (not reliable), ear (partial or total), articular (few), and any of the sections of costal cartilage which is the main source of supply. The cartilage may

be removed aseptically, if so desired; but this being unnecessary the cartilage is removed under clean conditions, completely cleared of any attached tissue and its perichondrium, washed with normal saline and then placed in a sterile container. The cartilage is then completely covered, by at least one inch, with a solution of one-part aqueous merthiolate (1–1000) and four parts of normal salt, called "merthiosaline," for purposes of identification. This container is then placed in the refrigerator in the hospital laboratory and left there continuously, being removed only when cultures are taken or the cartilage isograft is to be used for a transplant. After a new cartilage has been obtained, it is left in the original container for one week and then transferred, using aseptic precautions, to another sterile container and again submerged in the "merthiosaline" mixture. The "merthiosaline" solution should be changed every two to three weeks. The cartilage is not used unless the donor has a negative Wassermann, and until the isografts have had the refrigerated "merthiosaline" treatment for one week and two negative cultures have been returned. To date a positive culture has not been returned from the stored material covered with the "merthiosaline" and kept in the refrigerator as described above. I have used cartilage that has been stored for two years, but the cartilage that has been preserved six months or less is more satisfactory.

The cartilage isograft is very versatile in its application. I have used it to correct bony or cartilaginous defects of the head, face, chin, nose and orbital rim. On several occasions, due to depressed fractures of the orbit, I have used it subperiosteally in the floor of the orbit, as a wedge, to elevate the eyeball to its normal position. The cartilage of the pinna has been utilized *in toto* or in part for total or partial reconstruction of the external ear, following traumatic loss or congenital absence of the ear. It has proved of value as a supportive and contour element in ear reconstruction, and necessary in the restoration of deformed "cauliflower" ears to normal.

There are certain precautions that must be taken if one is to obtain the best possible result when using refrigerated cartilage isografts:

When the cartilage grafts to be used for transplants have been finally prepared they should be handled under the most aseptic conditions, not being touched by the gloved hand or permitting the cartilage to rub against the skin when introducing it into its recipient area. The pocket that is to hold the graft should be as close as possible a replica of the graft to be used, but the graft should not be under tension, so that all unnecessary dead spaces are eliminated and hemostasis of the area to be grafted should be complete. The grafts should be accurately splinted internally or externally, but preferably by both methods. These grafts may be used as replacement structures in fresh injuries only if the injury is of such a nature that one is justified in doing a primary closure, if the cartilage grafts can be completely covered without tension and if all of the requirements for the utilization of a free graft can be met.

In using refrigerated cartilage isografts, since the advent of the sulfa group of compounds, I have made an additional change in technic. All cartilage grafts are now used in conjunction with sulfanilamide locally. The grafts were first covered with the sulfanilamide powder and then placed in their bed. This made handling of the graft somewhat difficult, so at present the bed that is to hold the graft is completely covered with a fine film of the sulfanilamide powder blown in by an atomizer and then the graft placed in position. Although this is a relatively new development in technic, to date I have not had any untoward symptoms either locally or generally. In fact, the combination has definitely increased the conditions under which these grafts can be used.

The establishment and maintenance of cartilage depots can be accomplished with a minimum amount of effort and a negligible cost, and once established they would be of inestimable value to the surgeons who are called upon to do the reconstructive work.

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Original Articles

KELOIDS*

REVIEW OF THE LITERATURE AND A REPORT OF EIGHTY CASES

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THIS contribution is a report of eighty patients with keloids whom we treated in private practice and at the Department of Dermatology and Syphilology of the New York Post-Graduate Medical School and Hospital during the years 1929 to 1940. We have also reviewed the literature to date to facilitate discussion of the various phases of the subject of keloids, with special reference to theory and therapy.

Keloid was originally called cancroide.[1] Alibert first described keloid in 1814 as a "shellfish with processes like legs implanted into the skin." The name keloid is derived from the Greek χηλή meaning a claw.[2] The synonyms are cheloid, Alibert's keloid, kelis, Knollenkrebs in German and cheloides in French.[3]

Keloids are benign proliferative fibrous tissue overgrowths having their origin in the subpapillary plexus of the cutis and developing as a result of trauma. They are characterized clinically by hard, raised, shiny, usually smooth sometimes corrugated, hairless growths. They may be pink or red, white or brown according to their pigment content, vascularity and age. Their surfaces are often covered with telangiectatic capillaries. They may range in size from a quarter of an inch to several inches or more and may be oval, round, linear, irregular, in bands or ridges, bizarre shaped or button-like. (Fig. 1.) They form an abrupt transition and only rarely a gradual transition into the surrounding skin, frequently with claw-like prolonga-

FIG. 1. Case 78. Keloid on shoulder developed spontaneously (following pustule?). Keloid was excised and new button-shaped keloid developed which was later treated with *x*-rays. Post-treatment photo was lost.

tions. Keloids may be single or multiple, as many as a hundred or more, as shown by our Case 75 (Figs. 13, 14, 15 and 16) and as reported by de Amici.[4] They are usually situated in the longitudinal folds of the skin. They may be painful and tender and occasionally itchy. It may take months or even as long as twenty to forty years before they attain their maximum growth. Keloids have a frequent tendency to recur irrespective of the method used in their removal, whether by scalpel, electrosurgical knife, electrodesiccation, etc. In rare instances keloids may ulcerate, and they have been

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known to become malignant.[5] An unusually extensive case of keloids with ulceration and hyperkeratosis is described in special Case v.

Keloids are still classified as true and false. The former are also spoken of as spontaneous, genuine or idiopathic and the latter as secondary, spurious or cicatricial. The newer conception is that even the spontaneous keloids are caused by an injury so slight as to have escaped the attention of the patient, such as mosquito bites, pressure, scratching, irritation, comedos and infections. There is no difference pathologically between the spontaneous and secondary keloids.

ETIOLOGY

While an injury is the immediate cause of all keloids the primary reason for these growths is still unknown. There are probably a number of factors that interplay and are responsible for their production. The various theories that have thus far been advanced are discussed later in this article.

Among the predisposing factors age and race are known to play important rôles. Endocrine disturbances and increased hormonal stimulation or imbalance probably have a great influence in promoting these tumors. While keloids appear at all ages, they are most common in the young and rare in the aged. The greatest number of keloids in our series occurred between the ages of ten to twenty years. There were eleven in the first decade, twenty-three in the second, fourteen in the third, twelve in the fourth, five in the fifth, and two in the sixth, making a total of 67. In thirteen cases the age was not stated. There were forty-eight female and thirty-two male patients, the oldest being fifty-eight years. The duration of the keloids was from one to many years.

Naegeli[6] in an examination of 3,335 healthy school children found keloids in 151, an incidence of 4.5 per cent. Below the tenth year keloids predominated in boys, while between the ages of ten and fifteen years there was only a slight difference between the sexes. In 843 adults examined 118, or 13.3 per cent, had keloids. In 530 hospital patients of children and adults suffering from various acute and chronic diseases the incidence of keloids was found to be much higher than in healthy persons. In forty-nine patients with tuberculosis eleven, or 22.4 per cent, had keloids. The preponderance of keloids existed in vaccination scars. While these figures seem to be unusually high they may be explained by the probability that we included hypertrophic scars with keloids, thus enormously raising the percentage.

Negroes, Hindus and Malayans[7] are said to be more likely to develop keloidal growths than whites. The syphilitics and the tuberculous are likewise supposed to be more prone to develop keloids than others not so affected. Fox[8] found three cases of keloids in 3,382 white patients and seventy-six cases in 11,486 negroes, a ratio of negro to white patients of about 19 to 1. Hazen[9] saw one keloid in 2,000 white patients with cutaneous diseases but fourteen keloids in the same number of negroes. Matas[10] estimated the ratio of keloids in colored to white patients as 9 to 1. According to Grosse[11] this preponderance of keloids in the dark-skinned races is due to the practice of scarification in Africa, Australia, Polynesia, etc., for tribal, religious or sexual motives. While keloids are universally regarded as a disfigurement they are looked upon as beauty marks in Sudan, (Engelsen[12]) Malaya, Australia and other regions. In our eighty cases there were only three colored patients. This can easily be explained by the fact that very few colored patients apply for admission to our skin department and that white patients are more likely to seek advice and treatment for keloids.

The opinion that syphilis and tuberculosis are etiologic factors in promoting keloidal growths was not supported by our study. Thirty of our patients and seventy-eight out of 168 other patients with keloids of the Department of Dermatology of the New York Post-Graduate Medical School

and Hospital who had a Wassermann test taken gave negative serologic reactions. Among these patients (168 plus 80) only one was known to have syphilis. None of our patients presented clinical evidence of tuberculosis either in the bones, glands or lungs. Nine patients gave negative and three patients gave positive reactions to tuberculin in concentration of 1:10,000. This is within the normal limits. According to Martenson and Noll[13] 18.5 per cent of normal individuals react positively even in concentration of 1:1,000,000.

Keloids have a predilection for the sternum, back of the chest and lobes of the ears. The sternal region is the favorite location of spontaneous keloids (according to Smith[14] 50 per cent) where they are usually situated at right angles to the long axis of the sternum. However, no part of the body is exempt from keloid formation. Werner Schmidt[15] and Mook[16] reported keloids on the tongue. In Mook's case the keloid followed electrodesiccation of a wart.

In fifty-five of the eighty patients (67 per cent) the keloids were located on the upper half of the body. This is probably due to the greater exposure of that part of the body to injury and to the frequent occurrence of acne vulgaris on the face, chest and back. Keloids followed acne lesions in nine patients, or 11.2 per cent. There were three cases of spontaneous resolution. (Fig. 2.)

Fig. 2. Case 79. Illustrating keloidal scars following extensive burns with spontaneous regression without treatments within two years.

Fig. 3. Private case of Dr. George Miller MacKee. It illustrates keloids developing in herpes zoster lesions on the shoulder.

There is occasionally a family tendency to keloids. Gate and Coste[17] reported keloids in father and daughter. Similar occurrences have been reported by Wilson,[18] Hutchinson[19] and others. Hebra[20] reported keloids in a mother and her three daughters, Finsen[21] in two sisters, Neugebauer and Schramek[12] in three or four generations. In Case 54 (Table 1) father and daughter had keloids. Congenital keloids were reported by Bryant and Rosenthal.[12]

As already stated keloids may follow burns, cuts, bruises, surgical incisions, tattoo marks, acne, herpes zoster,[22] small pox, vaccinia, insect bites, etc. (Figs. 3, 4 and 5.) They may follow morphea, psoriasis, fibromas and lipomas.[23] A very unusual case of an extensive keloid developing spontaneously on a nevus (flammeus?) of the scalp is described in special Case IV. (Figs. 23 and 24.) Sutton and Sutton[24] show a remarkable photograph of a drug addict who presents numerous closely grouped match head-sized keloidal growths, most abundant on the ventral surfaces of the trunk and limbs. J. Margarot[25] reported a

case of a young woman with hyperthyroidism who developed keloids under the chin following electrolytic treatments for hypertrichosis. Her father also had keloids. One of our patients, a girl aged seventeen, developed keloids on the upper part of the left arm and shoulder two years after the removal of superfluous hair by electrolysis. Her father likewise was known to have keloids.

FIG. 4. Case 77. Showing keloids in both lobes of the ears after piercing for earrings.

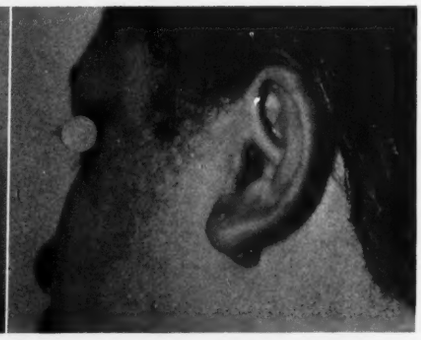

FIG. 5. Same Case 77 as in Figure 4.

Keloids may develop only in some out of many scars because of regional susceptibility. This is exemplified by our patient, a woman aged thirty-three, with congential syphilis (Figs. 6 and 7) who after a year of antisyphilitic therapy had a plastic operation performed for the absence of the columella and destruction of the nasal tip following a gumma. The flap was taken from the outer surface of the left arm. A keloid developed three months later on the arm at the area of incision but not on the nose during a period of two years. A similar case demonstrating local susceptibility was presented by Dr. Fox[26] at the New York Dermatological Society. The patient, a woman aged forty-three, developed keloids on the back, shoulders and sternum but not at the site of an appendectomy scar. Dr. MacKee in discussing this case stated that tendency to keloid formation is not necessarily generalized but may be limited to one part of the body.

Keloid formation may depend upon the nature of the irritant and character of irritation as demonstrated in Welander's case[27] in which keloids developed in tattoo marks tattooed red and not in those tattooed green.

Clare[28] suggests that some ovarian tumors may be looked upon as keloidal overgrowths of fibrous tissue. Schridde[29] describes keloidal lesions involving the throat, lung and stomach. He introduced the term "keloidosis," incorporating pneumonoconiosis and similar occupational lesions. Morison[30] states that keloids occur in the mouth as epulis, in the stomach as linitis plastica and in the cecum as hyperplastic tuberculosis in which the tubercle bacillus is not found. According to Bohrod[31] elephantiasis and fibrous stricture of the rectum may be due to a fibroplastic diathesis. Rectal strictures are known to be manifestations of lymphogranuloma inguinale; all the cases reported by Cole[32] and Bloom[33] gave a positive Frei reaction. However, since only some patients with lymphogranuloma inguinale develop esthiomene and rectal strictures, the fibroplastic diathesis or hormonal factor may conceivably be the underlying cause.

THEORIES

Sabouraud[34] was of the opinion that keloids are caused by the tubercle bacillus, stating that the "tuberculous nature of cheloids is beyond question." This was refuted by Pautrier and Glasser.[35] They ground up keloidal tissues from two patients with keloids and from one patient with acne keloid which they injected subcutaneously into the abdomen and intra-

dermally in the back of guinea pigs and rabbits. These animals were observed for months and no local nor general lesions were noted. Similar experiments were carried out by Naegeli,[36] Wartin, Drouet[37] and Marras[38] with negative results. Serologic tests with the antigen extracted from keloid tissue have given negative results as to the tuberculous element.[39]

Fig. 6. Case 76. Congenital syphilis, illustrating regional susceptibility to keloids. Keloid did not develop on the nose on which a plastic operation was done for absence of columella when seen at six months and a year later.

Fig. 7. Case 76. Showing a large keloid on the arm from which a flap was taken for the plastic operation on the nose.

Pautrier[40] attributes the formation of secondary keloids to the slow elimination of necrotic material and delayed epithelization. It thus prolongs the exposure of the collagen without the benefit of the protective, compensatory and stabilizing influences of the epithelial tissue. Similar ideas are promulgated by Lortat-Jacob, Fernet and Solenti.[41] They, too, attribute keloid formation to the loss or diminution of the protective influence of the epidermis, which acts as a control and normally exerts an antagonistic action against the proliferative properties of the derma. "When that action is diminished or lost the balance between the two antagonistic forces is disturbed so that even small stimuli are able to cause pathologic overgrowth of the true skin." These theories do not account for the keloids that follow even those wounds that heal by primary union (Fig. 8, Case 21) and in several of our other cases in which subepidermal sutures were used. These wounds, although they healed rapidly, were later followed by widening of the scar and keloid formation. Neither do these theories explain those cases of slow granulating, infected wounds of which only a fraction of 1 per cent develop keloids. Alibert[42] classified keloids as cancerous dermatoses, but keloids as clearly seen by histologic sections do not show the structure of an epitheliomatous degeneration. He may have formed his opinion by the crab and claw-like nature of these growths. An error might occasionally be made by the resemblance of the dense formation of the fibroblasts of the keloidal section to the spindle cells of sarcoma. Such an error was made in special Case III by the general pathologist who erroneously diagnosed the growth as fibrosarcoma.

Experimental evidence seems to link the glands of internal secretion to keloid formation especially the thyroid, parathyroid, thymus, ovaries, testes and spleen. Justus[43] believed that there is a close relationship between the thyroid gland and keloidal development. He induced keloidal growths in persons suffering from hyperthyroidism by irritating the skin "with

exitant pharmacologic substances, the activity of which was slight." Leriche and Jung[38] likewise reported that hard fibrous patches (keloidal?) in a woman patient gradually regressed following a unilateral resection of the inferior thyroid gland on that side. Balassa[38] noted that after the injection of thyroid extract following a thyroidectomy keloids were formed.

FIG. 8. Case 78. Illustrating recurrence of keloid in scar after excision.

Pautrier and Zorn[38] found a hypercalcemia in the blood and in the keloids in 75 per cent of cases (nine out of twelve) and a constant increase of this salt in all the keloid tissue. These findings lead Marras[38] to believe that keloid formation may be attributed to hyperparathyroidism which results in hypercalcemia. He believes that experiments and studies of the disease on disturbance of the calcium metabolism of the collagen tissue may solve the problem of the etiology of keloids.

Jung and Chinase Hakki[45] found hypercalcemia in four and normal calcium contents in five cases of spontaneous keloids. There was an increase of calcium in the keloid tissue as compared with normal connective tissue (0.221 to 0.654 in fresh tissue and 0.881 to 2.298 in dry tissue against 0.051 in normal skin expressed in mg. per cent, Nathan and Stern's micro method). However, with the MacCallum, Cretin, de Grandi and Mainini technic used for the purpose of studying the topographic distribution of the calcium it was revealed that there was a distinct decrease of the salt in the keloids as compared to the normal skin. This indicates that the calcium which is increased in the collagen of keloid tissue is calcium combined with albuminoid molecules, which can be revealed only by chemical methods respecting this combination but not by stains breaking up the intricate molecular structure.

In our most extensive case of keloids (Case 75, Figs. 13, 14, 15 and 16) the calcium content of the blood was normal, (10.1 mg. per 100 cc., the normal varying from 9.5 to 10.5 mg.).

Marras[46] found in several patients with keloids signs of endocrine dysfunction as exemplified by the residue of the thymus gland at the age of sixteen or by disturbed ovarian function. Crocker[47] stated that keloids are "uncommon in puberty." The possible association of keloids with ovarian or gonadal disturbance has been stressed by some writers because of the "presence of keloids before puberty and their absence or spontaneous resolution afterwards and the same coincidence before and after the menopause."[48]

These statements are contradictory; the second half "the same coincidence before and after menopause" coincides while the first half conflicts with the views expressed

by us at the end of this chapter where we associate the growth of keloids with greater hormonal concentration. During puberty and adolescence, because of the increase of hormones, a larger number of patients should develop keloids. This actually corresponds with our findings that the greatest number of keloids, 34 per cent, occurred during the second decade.

The relation of keloid formation to the spleen is suggested by the disappearance of keloids after splenectomy in a case of splenomegaly.[49] This may be due indirectly to thyroid or other hormonal influences because of the well known interrelationship between the ductless glands. Familial and hereditary influences on keloid formation is intimated by the many instances of familial occurrences that have been reported by Gate, Coste, Wilson, Hutchinson and other investigators as already cited, including our Case 54.

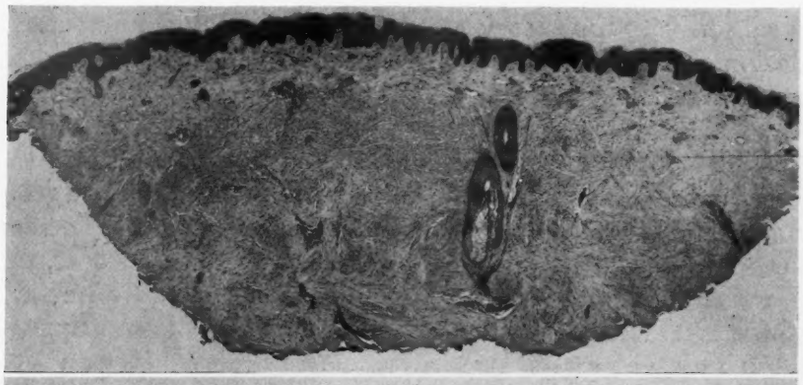

Fig. 9.

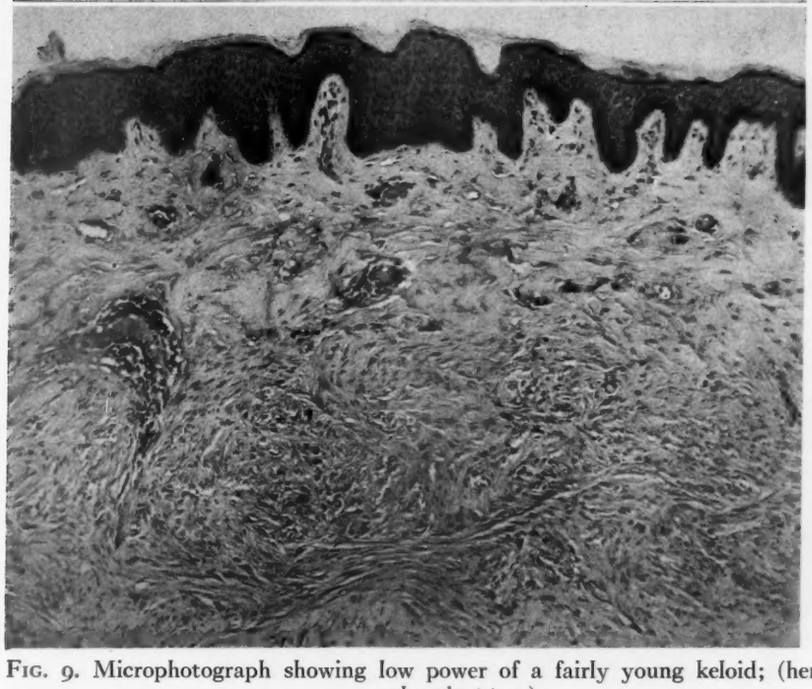

Fig. 10.

Fig. 9. Microphotograph showing low power of a fairly young keloid; (hematoxylin and eosin × 50).

Fig. 10. High power of Figure 9 (hematoxylin and eosin × 185).

Darier[50] regarded keloids as tuberculids while others thought that they are caused by a nontuberculous virus.[51] Bazin[52] attributed them to a fibroplastic diathesis. Kahler[53] considered them as a trophoneurosis or disturbance of innervation. Pautrier[54] states that "we must assume the lack or excess of certain cellular ferments or substances which we are still unable to define." Dystrophy of the elastic and collagenic

plexuses of the skin have likewise been mentioned as causes of keloidal growths.

COMMENT

We are willing to subscribe to the theory of hormonal stimulation as being the main or the important contributing cause of keloid formation. The fact that the largest number (twenty-three out of sixty-seven patients whose ages were given, 34 per cent) occurred in the second decade and the large percentage, 12 per cent, of keloids that followed acne vulgaris lesions would point to a hormonal factor as a likely cause for keloids because of increased glandular stimulation in the young. This view is further supported by the spontaneous resolution or absence of keloids after the menopause and by the rarity of keloids in the aged, possibly due to the diminution or disappearance of the male or female sex hormones.

DIAGNOSIS

The diagnosis of keloid is easily derived at clinically by the usual history of an injury; by its shiny, smooth, taut surface; by its location in the longitudinal folds and above the level of the skin; by the frequent presence of gradually diminishing ramifications and by the hard consistency. Histologically, there is a dense and well defined connective tissue new growth limited to the corium. In early keloids a great number of connective tissue cells are present while in older growths the mass becomes more dense and the cells more sparse. The microphotographs illustrate clearly the histologic structure of a young and an old keloid. (Figs. 9, 10, 11 and 12.)

Histologic Report of a Fairly Young Keloid of One Year's Duration (Dr. Sachs). Extending from the upper part of the cutis down to the bottom of the section are bundles of fibrous connective tissue, in some areas loosely arranged, in other zones compact. These bundles appear to run in various directions. About the periphery of the mass is a moderate number of dilated blood vessels some of which are filled with blood elements. There are a few dilated vessels within the connective tissue mass. The overlying epidermis is slightly acanthotic. The basal cell margin is intact and contains considerable pigment. The granular horny layer is present and apparently shows no change. There are no important changes in the rest of the epidermis.

Throughout the tumor mass is a moderate, diffuse, cellular infiltration. Most of the cells are large and spindle-shaped. They have a fairly large, vesicular, oval-shaped nuclei (fibroblasts). There is a slight amount of pigment in the upper cutis.

Histologic Report of an Old Keloid of Several Years' Duration. Extending throughout the entire cutis is a marked increase of connective tissue, the fibers being densely packed and arrayed in all directions. (Figs. 11 and 12.)

There are no adnexa in the section. In the upper part of the cutis there are a few small vessels which are moderately dilated. The epidermis is comparatively thin and other than a loss of rete pegs and papillary bodies shows no important change. Practically no cellular elements are present in the cutis. There are small fragments of elastic tissue throughout the entire mass.

DIFFERENTIAL DIAGNOSIS

While keloids have distinctive features and are usually easily recognized there are numerous instances in which a differential diagnosis has to be made between keloids and other raised nodular growths especially hypertrophic scars, sarcoids, scleroderma, fibroma and paraffinomas.

Both keloids and hypertrophic scars are due to trauma and both have their origin in the corium. Hypertrophic scars, however, do not extend beyond the original boundaries of injury, while keloids tend to extend into neighboring tissues usually forming claw or fringe-like projections. Hypertrophic scars are not usually elevated more than one-sixth of an inch (0.4 cm.) above the surrounding skin surface while keloids may reach the size of several inches. (Figs. 21 and 22.) In hypertrophic scars the

overlying epidermis is atrophic, the epidermodermal junction flattened and new collagen bundles are formed in the papillary and subpapillary layers. In keloids the hypertrophic change begins in the middle of the corium and spreads slowly toward the surface, sparing the capillary layer and giving room to little if any appreciable changes in the epidermis.[55] Hypertrophic scars, especially those after burns, are much more transitory than keloids and may undergo spontaneous healing, while keloids only rarely regress spontaneously.

The superficial sarcoids have a yellowish-brown tinge. Sarcoids located on the face have a bluish center and a yellowish border. Diascopic pressure shows the nodules as grayish-yellowish foci. They are usually anergic to intracutaneous tuberculin injection. There may be lung, bone, eye and other tissue involvement. Histologically, the epithelioid and cell nests of the corium

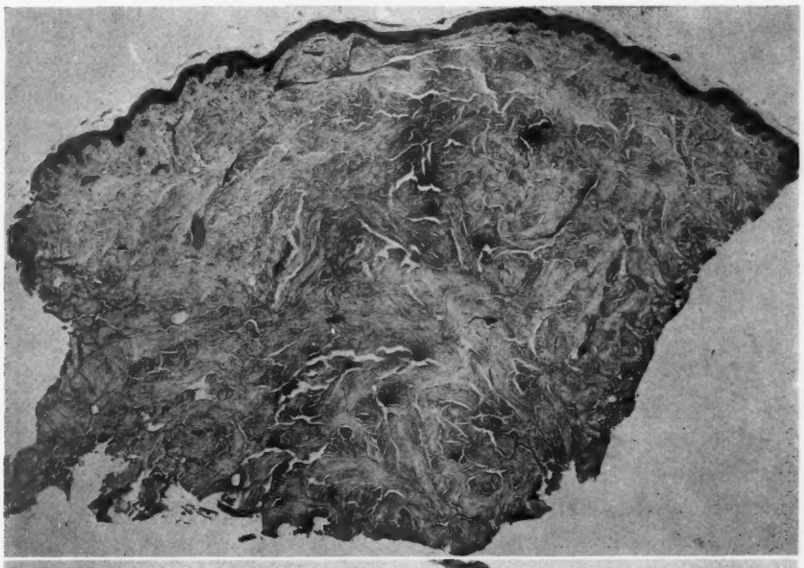

Fig. 11.

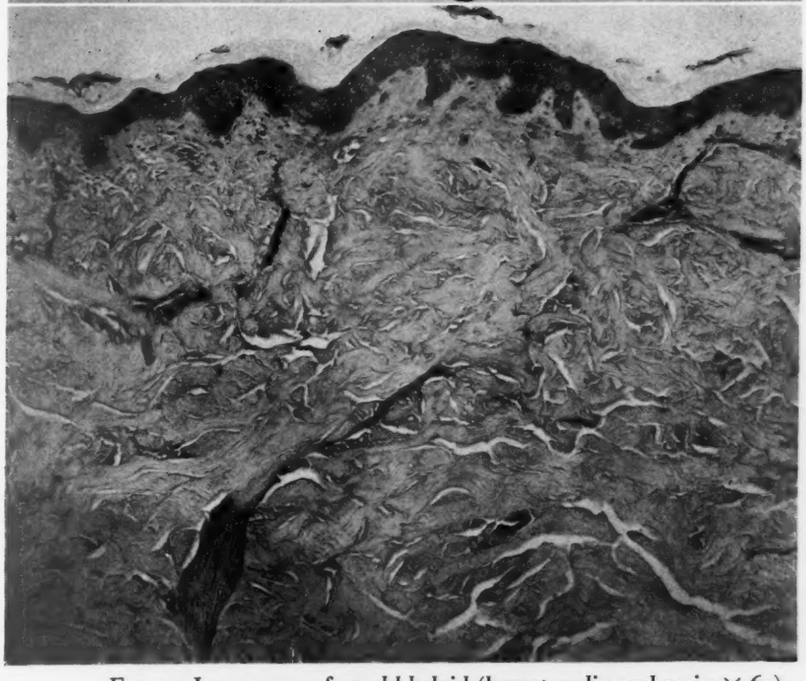

Fig. 12.

Fig. 11. Low power of an old keloid (hematoxylin and eosin × 60).
Fig. 12. High power of Figure 11 (hematoxylin and eosin × 185).

separated by connective tissue septa are very characteristic. The elastic and collagen fibers are completely destroyed throughout the entire growth.

Scleroderma is markedly infiltrated and lardaceous. The center has the color of ivory. The border of a typical patch is distinctive. It is made up usually of a narrow zone consisting of a plexus of fine vessels which impart to it a pinkish-lilac or violaceous hue. Histologic examination reveals that the hardness is due to a thickening and increase in density of the collagen bundles and not to new formation of fibrous tissue. It shows an altered affinity for dyes as revealed by van Gieson preparations which stain sclerodermatous tissue reddish-brown while normal collagen stains red. The elastic tissue may be diminished but does not show the degenerative changes found in the atrophic diseases of the dermis.[56]

Fibroma durum occurs as a firm reddish nodule which may reach the diameter of 1 cm. They are usually located on the legs and may rise slightly above or be somewhat depressed below the general surface. Histologically, they are found to be composed of interlaced bundles of cellular fibrotic tissue separated from the overlying epidermis by a narrow margin. The collagen bundles have lost their normal form and arrangement and are rich in nuclei. They are narrower than normal and stain more deeply with eosin. The normal structures of the skin are usually entirely absent.

Paraffinomas occasionally resemble keloids, but their usual location on the face, their softer consistency and the history of previous paraffin injections serve to distinguish them from keloids. A histologic section would reveal the very typical swiss-cheese-like character of paraffinoma.

It is necessary to define the term cure as applied to keloids. Young and small keloids will disappear with a few subintensive, three-quarters of the erythema dose, (337 r for the 1 mm. and 412 r for the 3 mm. aluminum filter) *x*-ray exposures with little or no disfigurement but large and old keloids will require numerous filtered roentgen treatments for their resolution. The cure in the latter will consist of a soft and pliable scar with some atrophy and, perhaps, some telangiectasia.

An *x*-ray unit with a mechanical rectifier was used in the clinic and a valve tube machine in our private offices. Since the erythema doses today are calculated in roentgen units, an exact administration of *x*-ray doses is everywhere assured. For unfiltered radiation the factors for the erythema dose were as follows: 100 kilovolts (6 inch spark gap), 3 milliamperes, 2 minutes, 8 inch distance from target to object. This equals 300 roentgens.[57] For filtered radiation through 1 mm. aluminum the factors were 137 kilovolts (9 inch spark gap), 5 milliamperes, 10 inch distance 3.75 minutes. This equals 450 roentgens. For filtered radiation through 3 mm. aluminum the same factors were used as for 1 mm. aluminum but for a period of 7.5 minutes. This corresponds to 550 roentgens.

SPECIAL CASES

A brief description of some of the interesting cases has already been given in this paper or included in the charts. The following five cases deserve special descriptions:

Special Case 1. The most unusual case in our series is that of M. Z., aged sixten, Case 75. (Figs. 13, 14, 15 and 16.) She registered at the skin department on October, 1935, with lesions on the face, neck, back and chest of four years' duration. There were numerous comedons, papules and pustules; also pea to coin-sized, discrete and confluent, smooth, shiny, well defined, hard growths, some assuming gyrate forms. On the surfaces of many of the keloids were numerous telangiectatic capillaries. She was treated prior to her admittance at the clinic with fifteen superficial *x*-ray exposures in 1934, 0.25 units each, without any result. The blood calcium was 10:1 mg. per 100 cc. of serum (normal 9.6–11.0). Old intracutaneous tuberculin test in concentration of 1:10,000 was negative. A roentgenogram showed a relatively small spherical heart and moderate cen-

No.	Name, Age, Sex, Race	Date of Admission	Duration	Cause	Description	Treatment Given	Result	Important Findings
2	T. E. 30 F. W.	5/11/31	Five years	Recurred after excision	Two cm. sized keloid on front of chest.	Keloid was excised and subcutaneous dermal sutures used. The healed wound was then exposed to 6 genz rays 0.5 skin unit each. The keloid recurred. Two *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum were given once a month. (Total 825 r.)	Cured	Failure of subepidermal sutures and 3 units of grenz rays to prevent recurrence. Cured after filtered *x*-rays.
4	S. M. 11 F. W.	4/19/33	Two years	Dog bite cauterized with nitric acid	5 by 4 cm. linear keloid on upper arm.	Eight *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum at first, then through 2 mm. aluminum every 4 weeks. (Total 3300 r.)	Cured	Cured after filtered *x*-rays.
5	C. F. 58 M. W.	10/ 2/31	Four months	Removal of senile keratosis	Finger nail-sized keloid on chest.	Four *x*-rays unfiltered skin units 0.5 each. (Total 600 r.)	No response	No response after 2 units of unfiltered *x*-rays even on young keloids.
7	G. L. 40 F. W.	11/30/33	Five years	Not stated	7.5 cm. keloid on right side of neck.	Three *x*-rays skin unit 0.75 each filtered through 1 mm. aluminum. (Total 1012½ r.)	Cured	Cured after *x*-ray therapy.
8	F. J. 9 F. W.	10/ 7/32	Nine months	Scalded	Dollar-sized keloid on chest.	Eight *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum. (Total 3300 r.)	Cured	Cured following filtered *x*-ray therapy.
10	R. R. 35 F. W.	9/23/33	Three years	Boils	Keloid on right shoulder.	Six *x*-ray skin unit 0.75 each filtered through 1 mm. aluminim once a month. (Total 2475 r.)	Cured	Cured after sufficient filtered *x*-ray therapy. Tuberculin test positive in dilution of 1:10,000.
12	G. F. 24 F. W.	3/26/31	Seven weeks	Followed acne cysts	Keloid on right cheek.	Destroyed by electrodesiccation, but it recurred. Then 14 *x*-rays skin unit 0.25 each unfiltered were given once a month. (Total 1050 r.)	Slight improve-	Keloids followed acne cysts. It recurred after electrodesiccation. It responded only slightly to unfiltered *x*-rays.
13	M. F. 11 M. W.	6/26/39	Two years	Post-operative	Post-operative in right inguinal region.	Four *x*-rays skin unit 1 each unfiltered were given once monthly (total 1200 r). There was no response. It was then destroyed by electrodesiccation but it recurred. Four roentgen treatments 0.87 units each filtered through 1 mm. aluminum were given to umbilical and 5 such does to the inguinal region. (Total 1575 and 1969 r respectively.)	No response to 4 skin units of unfiltered *x*-rays. Cured with filtered radiation.	No response to 4 skin units of unfiltered *x*-rays. Cured with filtered radiation begun 20 days after electrodesiccation.

No.	Name, Age, Sex, Race	Date of admission	Duration	Cause	Description	Treatment Given	Result	Important Findings
14	L. A. 6 F. W.	12/ 4/33	Two years	Burn by fire	Multiple keloid on face, chest, neck and shoulders.	Seventeen *x*-rays unfiltered 0.25 skin unit each once weekly. (Total 1275 r.)	Very good result	Negative tuberculin tests in all concentrations. Reexamined on August 25, 1940, very good result.
18	N. E. 19 M. W.	11/10/31	One year	Followed electrodesiccation	Small pea-sized keloids over sternum.	Eight *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum every 4–6 weeks. (Total 3300 r.)	Cured	Recurrence after electrodesiccation. Cured after sufficient filtered *x*-ray therapy.
19	B. M. 11 M. W.	8/ 8/31	One year	Burned	Palm-sized keloid over left pectoral area.	Three *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum once monthly. (Total 1237½ r.)	Cured	Cured
20	C. J. 18 F W.	7/14/28	Ten months	Fibroma molle fulgurated followed by electrolysis to scar	Keloid on chin.	Three *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum once monthly. (Total 1237½ r.)	Fair response	Keloids followed electrolysis treatment for scar. Fair response to filtered *x*-rays.
21	K. A. 30 F. W.	11/13/32	Six months	Excision of growth	Keloid on right wrist.	Fourteen *x*-rays skin unit 0.75 each unfiltered once weekly. (Total 1050 r.)	Poor response	Widening of scar even in clean wound.
23	M. L. 34 F. W.	6/20/32	One year	Pigmented nevus removed with acid	Two keloids 0.6 cm. each on left cheek.	Eight *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum at first and then through 1 mm. aluminum. (Total 3637½ r.)	Cured	Cured after sufficient filtered *x*-ray therapy. Keloid followed treatment of nevus with acid.
24	D. R. 7 F. W.	1/13/32	Three years	Cause unknown	Two keloids 7.5 cm. and 3.1 cm. on left shoulder and arms.	Eight *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum every 6 to 8 weeks. (Total 3300 r.)	Cured	Cured with filtered *x*-rays.
25	D. N. 34 M. W.	7/ 1/32	One year	Injury	Linear 6 by 4 cm. keloid on right cheek.	Seven *x*-rays exposures skin unit 0.5 each filtered through 3 mm. aluminum, last 2 treatments given through 1 mm. aluminum. (Total 2475 r.)	Slow response	Resistant to filtered *x*-ray therapy.
26	S. E. 16 M. W.	2/ 2/30	Three years	Acne vulgaris	Numerous pea and larger-sized round irregular keloids on chest.	Five grenz rays skin unit 0.5 each. Then 6 *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum, followed by skin unit 0.5 through 3 mm. aluminum. (Total 2475 r).	Cured	Keloid followed acne cysts. Five grenz rays skin unit 0.5 each failed to have any effect, but filtered *x*-rays resulted in cure.

No.	Name, Age, Sex, Race	Date of Admission	Duration	Cause	Description	Treatment Given	Result	Important Findings
31	F. F. 20 M. W.	10/24/31	Four months	Burn	Pea-sized raised hard growth on left arm.	Three *x*-rays skin unit 0.75 each filtered through 1 mm. aluminum once a month. (Total 1575 r.)	Cured	Keloid followed a verrucous lesion that was desiccated.
32	F. A. 42 F. W.	10/22/31	Six months	Small verrucous lesion desiccated	Three keloids on arm, axillae and breasts following scald.	Six *x*-rays skin unit 0.75 each unfiltered and 5 *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum. (Total 2062 r.)	Cured	
33	K. I. 22 F. W.	12/30/28	Two years	Scalded	Two keloids 2.5 cm. and 1.5 cm. in size on chest.	Three grenz rays 0.5 units each every 2–4 weeks, no change. They were then exposed to *x*-rays skin unit 1 each, filtered through 3 mm. aluminum and 3 *x*-rays skin unit 1 each filtered through 3 mm. aluminum. (Total 6187½ r.)	Very resistant not much change	Keloid resistant both to grenz rays and to 6187 units of filtered roentgen rays.
34	Q. M. 18 M. W.	1/29/34	Three months	Cause unknown	Dime-sized keloid on chest.	Seven *x*-rays unfiltered skin unit 0.25 each (total 525 r). Then followed by 5 *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum. (Total 2062 r.)	Cured	No change with unfiltered. Good progressive response with filtered *x*-rays. Keloid followed lesion of acne vulgaris.
35	M. B. 38 W. F.	10/27/33	Three months	Dessiccation of baso-spinal cell epithelioma	One keloid on forehead.	Four *x*-rays unfiltered skin unit 0.5 each. (Total 600 r.)	Good response	Keloid followed electrodesiccation. Good response with 2 units of unfiltered *x*-rays.
41	W. M. 17 F. W.	8/ 9/31	Four months	Burn	One light keloid on cheek.	Ten *x*-rays unfiltered skin unit 0.5 each once every 2 weeks. (Total 1500 r.)	Cured	Cured with unfiltered *x*-rays because keloid was young.
42	V. M. 11 F. W.	9/15/31	Five months	Nevus unius lateralisdesiccated	Quarter-sized keloid on side of neck.	Six *x*-rays skin unit 0.75 each filtered through 3 mm. aluminum every month. (Total 2475 r.)	Cured	Keloid followed electrodesiccation.
54	F. E. 17 F. W.	4/15/35	Two years			Six *x*-ray skin unit 0.75 each filtered through 3 mm. aluminum every 3 weeks. (Total 2475 r.)		Keloids followed electrolysis for removal of superfluous hair.

No.	Name, Age, Sex, Race	Date of Admission	Duration	Cause	Description	Treatment Given	Result	Important Findings
75	Z. M. 18 F. W.	10/ 2/35	Four years	Acne vulgaris	Multiple pea- to dime-sized and larger keloids on face, chest, neck and back.	Twelve *x*-rays skin unit 0.25 each unfiltered. (Total 900 r.)	No change	Negative to tuberculin in all concentrations. This is the most extensive case of keloids in our series. They did not respond to any form of therapy. (Special case 1, Figs. 13, 14, 15 and 16.)
76	F. A. 40 F. W.		Three months	Flap for plastic operation	One linear keloid on left arm	Filtered *x*-rays.		Congenital syphilis. Keloid developed on arm from which flap was taken but not on the nose on which plastic operation was done. Case serves to illustrate regional susceptibility. (Figs. 6 and 7.)
80	J. C. 12 M. C.			Retro-auricular keloid followed cut by ax keloid on deltoid region followed vaccination	Large keloid behind right ear also on left deltoid region.			See description of special case III. Fifty per cent regression of large keloid on deltoid region within 3 years.

tral and slight interlobar, pleural thickening. An area on the right shoulder corresponding to the outline on the photograph (Fig. 16) was treated with the following methods without showing any improvement: Forty injections of fibrolysin intrakeloidally for a period of six months; negative and positive poles of a direct or galvanic machine using 1.5 milliamperes for 2 minutes, six treatments of each. One large keloid was treated with several through-and-through black sutures. Two small lesions were treated with four solid carbon dioxide snow applications. The patient also took thyroid extract orally 0.25 Gm. and thiosinamine, 0.1 Gm. each three times a day for six months. She kneaded the keloids frequently with cocoa butter.

Special Case II. A. L., aged six, Case 14 (Figs. 17, 18, 19 and 20) registered at the skin clinic on December 4, 1935. She presented extensive keloids of two years' duration on the face, neck, chest, shoulders and upper extremities following severe burns in an explosion. She was treated with seventeen unfiltered *x*-rays, 0.25 units each, once weekly. Examination on January 30, 1942, showed that the keloidal growths on the face and nose were flattened and the skin was white in color. Those on the flexor surface of the neck were brownish-red, very pliable and did not interfere with the movements of the head. The keloids on the shoulders and extensor surfaces of the arms were decidedly improved. Considering the marked disfigurement which the patient presented when first seen, this should be considered a very good result.

Special Case III. F. C., a nine year old colored boy, developed in 1934 a large keloid behind the left ear following a cut with an ax. A similar-sized keloid developed on the left deltoid region following a vaccination. Within a period of three years the retro-auricular growth was thrice excised by a surgeon but it recurred soon after. (Figs. 21 and 22.)

After the last excision the surgeon repaired the wound with a full thickness skin graft taken from the abdomen. The grafts failed to take and the keloids developed behind the ear and on the abdomen.

On December 17, 1937, the authors exposed the growths behind the left ear and on the abdomen to filtered *x*-rays, 200 r every four to eight weeks, receiving a total of about 5 units (200 r). After three months the keloids on the abdomen gradually began to regress and became soft, wrinkled and flat. Three months later the keloid behind the left ear began to undergo involution. The keloid on the left deltoid region which was not exposed to *x*-rays also became softer and shrank to one-half of its original size.

This is an example of the tendency of colored patients to have large keloids. It also illustrates the futility of surgical removal of a keloid unless it is followed by roentgen treatments at the first sign of recurrence.

The regression of the keloid on the left deltoid region may have been due to spontaneous resolution or to the indirect effect of the roentgen rays applied to the retro-auricular region, similar to the result obtained by Niles[58] in acne vulgaris when in many patients the untreated side of the cheek cleared up as soon and as completely as the side that was treated with *x*-rays.

Fig. 13. Case 75. Special Case I. Illustrating multiple keloids on face, chest and back in acne lesions.

Special Case IV. L. T.,[58] a girl aged eighteen, registered at the Skin and Cancer Unit on June 20, 1940. She had a triad complex of adenoma sebaceum, tuberose sclerosis and epileptiform seizures. She presented a large disfiguring growth on the scalp and a crimson-red eruption on the face. She had a flat purplish-red nevus on the scalp since birth. At nine years this nevus (flammeur?) began to develop into a hard, painless growth. It continued to grow for seven years and then it became stationary. It was almost hairless, flesh-colored to reddish, 18.7 cm. in length, 2 cm. to 1 cm. in depth and 5–8.8 cm. in width. (Figs. 23 and 24.)

Fig. 14. Case 75. Special Case I. Showing numerous keloids on front of chest and breasts.

The entire growth was removed in two operations by Dr. Straatsma and a plastic repair done. The flaps were taken from the thigh and flank. A section examined by Dr. Rabson and Dr. Satenstein showed the histologic structure of keloid. Van Gieson stain failed to reveal any neural tissue.

Fig. 15. Case 75. Special Case I. Illustrating the presence of hundreds of small keloids on the back of the chest.

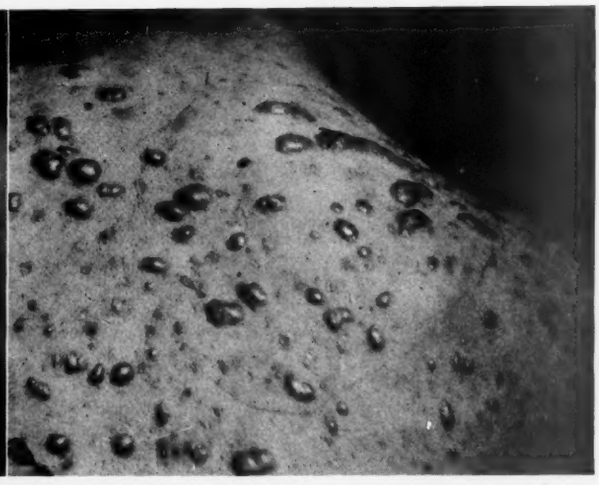

Fig. 16. Case 75. Special Case I. Illustrating a section of the back on which numerous methods of treatment were done including forty injections of fibrolysin without any benefit.

Special Case V. Mrs. M. J., a woman aged forty-nine, applied for treatment as a private patient on March 1, 1942. She gave a history of having scalded her nates and thighs about fifteen years ago with hot water. Physical examination revealed extensive keloidal growths involving both buttocks and lower part of the back with hypertrophic scarring of the flexor surfaces of the thighs. On the right buttock were several punched-out, irregular ulcerations varying from 0.1 to 1 cm. in depth, 1 to 3 cm. in width and 5 to 10 cm. in length. The floors were fairly even, necrotic, secreting some slight seropurulent discharge. Some of the keloidal areas were covered with dry, dark brown, hard, hyperkeratotic patches. Two sections taken from the latter were examined histologically by Dr. Satenstein and diagnosed as keloids. The epidermis was thickened and the horny layer increased. There was no evidence of any malignancy in the epidermis. The cutis showed an increase in the collagen bundles and fibroblasts.

Fig. 17. Case 14. Special Case II. Illustrating extensive keloidal scars and bands, interfering with the movements of the neck following burns in an explosion at eight years of age.

Fig. 18. Case 14. At eight years of age, showing large keloidal bands on the right side of the neck.

ANALYSIS OF THE CASES TREATED

We treated forty-six female and thirty-four male patients, three of which were colored. They ranged in age from two to fifty-eight years. None of fifteen patients gave a personal history of tuberculosis. Intracutaneous tuberculin tests were made on nine patients. All of them gave a negative reaction to the tuberculin in concentration of 1:100,000, three of these giving 3 to 4 plus reactions to 1:10,000. The keloids were located mostly on the upper part of the body. They varied in color from yellowish-white to purplish-red and in duration from one month to many years. Nine cases followed lesions of acne vulgaris; eight, electrodesiccation, two cauterization with acids, and one after ultraviolet exposure. Two cases followed the piercing of the ear lobes for earrings (Figs. 4 and 5), and one case with multiple keloids on the chin followed electrolysis for hypertrichosis. All seven keloids that were excised recurred. There was a tendency to spontaneous resolution in three patients.

Only one of six patients showed some improvement after 4.5 units of infra-roentgen (grenz) rays. Three units of grenz rays failed to prevent recurrence in Case 2. One patient responded well to 4 and another to 5 units of unfiltered *x*-rays which were given soon after recurrence (Cases 37 and 41). Twenty patients were cured by filtered radiation. Two patients were very resistant to large doses of *x*-rays. One patient (Case 25) did not respond to 2475 and another (Case 33) to 6187 r units.

FIG. 19. Case 14. Showing the good result at the age of fourteen. These bands are soft and pliable.

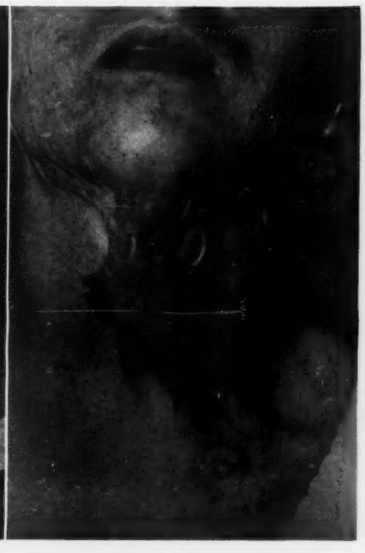

FIG. 20. Case 14. At fourteen years of age. Keloidal scars are now pliable. She is able to move her head freely in all directions.*

Keloids that were treated regularly soon after occurrence of recurrence responded well to comparatively small doses of *x*-rays. One patient, special Case 1, did not show the slightest response to any form of treatment known to us.

TREATMENT

Keloids have been treated with internal medications, topical applications, physiotherapeutic methods and surgical procedures. Iodine, mercury, arsenic, quinine, strychnine, potassium iodide and thiosinamine have been used internally without any apparent benefit. Similarly useless are the various topical applications of which only the pepsin-boric acid method of Unna

*The keloidal bands of the neck were excised at the New York Post-Graduate Hospital in September, 1942. We feel that the patient had probably already lost the keloidal tendency. She is being watched very carefully. *X*-ray treatments will be given at the first sign of occurrence of the keloids.

need be mentioned which had for its purpose the softening and reduction in the size of keloids through lengthly applications. The intrakeloidal injections of any water or oily solution are to be condemned as being painful and useless. Numerous injections of fibrolysin have been given in our special Case 75 and in our private practices without the slighest change.

Fig. 21. Case 80. Special Case III. A large keloid developed behind the right ear following an ax cut.

The physiotherapeutic methods of cryotherapy (refrigeration), electrolysis with negative or positive poles, ultraviolet rays water-cooled (Kromayer) and grenz rays are useless. Iontophoresis with solutions of potassium iodide, sodium salicylate, resorcin in various d.lutions as tried by us and on eight patients by Lerner[59] did not produce any beneficial results.

Among the surgical methods used but proved ineffective by the authors are scarification with the scalpel, capillary drainage by means of through-and-through keloidal sutures, and subepidermal excision for the purpose of causing primary union.

Roentgen rays and radium are the only effective treatments for keloids and will cure most of them except those that are radioresistant.

For large keloids and those that are resistant to a sufficient amount of filtered *x*-rays and radium, excision in the healthy tissue by the scalpel or electrosurgical knife (acusection) is preferred. The healing should be promoted by aseptic technic and the use of stimulating substance such as scarlet red salve. Roentgen therapy should be applied at the first sign of recurrence, but not until then as irradiation before and soon after excision will not prevent the formation of keloids.[60]

Fig. 22. Case 80. Large keloid on left deltoid region followed vaccination. It recurred after excision. This keloid regressed 50 per cent without treatment during the age of twelve to fifteen years.

Filtered roentgen therapy is the treatment of choice. The exact dose will depend upon the location, duration, thickness, size of the keloid and the age of the patient. For small keloids one-quarter of a skin unit weekly filtered through 1 mm. aluminum (112.5 r), or one-half unit (225 r) every two to three weeks may be given, the lesions being closely shielded with lead foil up to a total of 2 to 3 units (900–1350 r). For larger and thicker keloids one-half to three-quarters of a skin unit (subintensive) filtered through 3 mm. aluminum (275–412.50 r) should be given every three to four weeks. Six to eight such subintensive doses are usually necessary for a good re-

sult. Twelve such doses may be considered as the maximum that could be used but only in exceptional cases.

While it is generally recognized that young keloids respond better than old keloids to radiation it has been our experience that some young keloids will require even more roentgen treatments than older keloidal growths. This can be explained by the fact that in early keloids the stimuli which are responsible for their development are not sufficiently counteracted or suppressed by the average amount of roentgen ray treatments and a dosage of about 5 erythema doses is required for their cure.

Biokinetic massage and kneading with cocoa butter is a very useful procedure in conjunction with *x*-ray and radium treatments and is especially indicated for hard and extensive keloids that interfere with the motion of joints.

Radium is to be used for small keloids that are inaccessible to *x*-rays. Soft or beta radiations may be applied for fresh and superficial keloids and hard gamma rays for keloids that are more than 1 or 2 mm. in thickness. A half strength, glazed, flat applicator screened with 0.1 mm. aluminum and shielded with two layers of rubber tissue may be placed in contact with the superficial keloid for ten to twenty minutes depending upon the age of the patient and location of the lesion. This may be repeated once every four to six weeks for about six treatments.

For lesions above 1 or 2 mm. in thickness gamma rays are preferable. A half-strength flat applicator may be screened with 1 mm. of brass and 3 mm. of rubber and placed in contact with the lesion for eight to twelve hours, applied at one time or in several visits one to two hours a day. In some instances it is advisable to cross-fire with a combination of *x*-rays and radium. For example, in a deep-seated keloid in the cheek radium may be placed in the mouth and *x*-rays applied to the external surface of the cheek.[61]

Mention should be made here of the prevention of keloids. Patients who are susceptible to keloidal growths should be advised to avoid irritation and trauma, such as sunburn, tight belts, etc. Special attention should be given to the treatment of acne, furunculosis, herpes zoster and other skin diseases that may result in keloid formation.

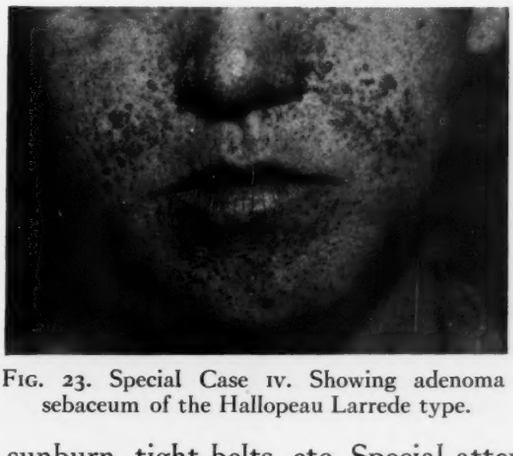

Fig. 23. Special Case IV. Showing adenoma sebaceum of the Hallopeau Larrede type.

SUMMARY AND CONCLUSION

Most keloids are caused by a known trauma. Even spontaneous keloids are thought today to result from an injury which may have been so slight as to have been overlooked by the patient.

Our studies do not show that syphilis and tuberculosis are etiologic factors in the production of keloids. There was only one case of known syphilis in 248 patients from our series, from the Department of Dermatology of the Post-Graduate Medical School and Hospital and the Skin and Cancer Unit, and even that patient showed only regional predilection for keloids.

Special emphasis has been placed on the glands of internal secretion as possible factors in keloidal growth. The greater percentage of keloids (34 per cent) in the second decade of life, the larger number (12 per cent in our series) that follow acne vulgaris lesions and the rarity of keloids in the aged, perhaps as a result of spontaneous resolution due to diminution or absence of hormonal secretion, point to a hormonal factor as the possible cause of keloidal growths.

Hyperparathyroidism which causes hypercalcemia has been regarded as a factor in promoting keloidal growths by causing an increased calcium content in the tissues. However, with special stains that break up the albuminoid molecule which is combined with the calcium it was found that there was an actual decrease of calcium in the tissues.

Epulis, some tumors of internal organs as in the throat, lung, stomach or ovaries, and even esthiomene and rectal strictures are looked upon by many investigators as forms of keloidal growths.

Although keloids have distinctive characteristics and are ordinarily easily diagnosed, there frequently arises the question of differentiating keloids from other growths and a resort to histologic section is obligatory.

Primary union of a growth does not prevent the formation of keloids. Treatment with roentgen rays or radium before or soon after excision of a keloidal growth does not prevent its recurrence.

The sooner the keloid is treated the better is the result, though some young keloids require even more roentgens than older keloids to effect a cure. A keloid of sufficient size should be first excised by the scalpel or surgical knife, the wound healing hastened and *x*-ray or radium applied at the first sign of recurrence.

FIG. 24. Special Case IV. Showing large keloidal growth on the scalp which was removed later by Dr. Straatsma in two operations, flaps being taken from the flank and the thigh. The result has been good.

Among the special cases described two patients are of particular interest: one a girl aged eighteen, with hundreds of keloids that did not respond to any form of therapy and another, a woman aged forty-nine, with extensive keloidal growths of fifteen years' duration who developed deep ulcers and hyperkeratotic areas.

Various treatments as medications *per oram*, intrakeloidal injections, physiotherapeutic and surgical methods have been mentioned to discard those proved worthless and to recommend those found to be of value.

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TREATMENT OF BLOOD STREAM INFECTIONS WITH HEMO-IRRADIATION

CASE REPORTS

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IN 1934, the June issue of Northwest Medicine contained an article by this writer and E. K. Knott, entitled "Irradiated Blood Transfusions in Treatment of Infections." Since that time, several articles have been published by various writers on research phases and clinical responses to this same treatment. This modality is generally spoken of as hemo-irradiation. It is the purpose of this paper to review briefly the widened rationale as well as to report further on the writer's experience with this therapy in the treatment of blood stream infections.

Hemo-irradiation therapy consists of exposing a part of the patient's blood to ultraviolet rays. A predetermined amount of the patient's blood is withdrawn from a vein and citrated. The blood is then strained into a transfusion graduate and returned to the same vein through an air tight conduit. A specially designed irradiation chamber with a quartz window is connected into the conduit. The chamber is about two inches in diameter and approximately one inch thick; it has an inlet and outlet, and connecting the two is a labyrinthine passage formed by baffle plates which are ground to fit flush against the quartz window so that the blood must flow around instead of across them. As the blood passes through the channels of this chamber it is exposed to ultraviolet rays generated by a water-cooled mercury vapor quartz burner. The distance from the source of the ultraviolet, or the burner, to the blood is approximately 3 cm. The period of time of exposure for each cc. of blood, the total volume of blood irradiated and the frequency of treatment are determined by the pathological status and the patient's condition. The volume of blood irradiated at any one time is generally determined by the patient's weight and condition; usually about one-twelfth to one-sixteenth of the blood volume is treated.

There has been no basic change of procedure since 1933. Research, however, has brought about certain modifications of technic. The design of the irradiation chamber is greatly improved, giving a more uniform exposure to all parts of the blood. There has been developed an electrically synchronized irradiation machine that regulates exactly the rate of flow of the returning blood and the time of exposure.

Originally, hemo-irradiation was developed to try to utilize the bactericidal properties of ultraviolet rays by directly irradiating the blood stream and thereby combating blood stream infection. This idea was developed successfully, but clinical observations on patients treated indicated that several other biological and biochemical reactions were taking place within the patient with decidedly beneficial results ensuing. The reactions observed in various conditions have been subjected to critical investigation for several years.

This research in a wide variety of conditions, and the method of administering treatment developed by E. K. Knott have resulted in the procedure known as the Knott Technic. This technic of applying ultraviolet rays of selected wave lengths and intensity and the time of direct exposure of the blood for the treatment of infections gives us, I believe, a therapy of more pronounced merit than any other to date. It is essential, however, that for uniform

and satisfactory results, the Knott technic be strictly adhered to.

A rational foundation that led to the development of hemo-irradiation was established on published scientific data on the biological and biochemical reactions of ultraviolet irradiation. All of the points of the rationale are facts that have been substantiated by several recognized authorities working independently. Some of the most important underlying principles of this procedure are based on the fact that ultraviolet irradiation by selected wave lengths and correct exposure causes: (1) An inactivation of toxins and viruses;[1,2] (2) destruction and inhibition of growth of bacteria;[3,4] (3) increase in the oxygen combining power of the blood;[5] (4) activation of sterols resulting in production of vitamin D;[6] (5) increased cell permeability;[7] and (6) an absorption of ultraviolet by the blood and emanation of secondary radiations.[8]

There have been many demonstrations of the inactivation of toxins and viruses *in vitro* by ultraviolet rays. The work on snake venom by Noguchi[10] who inactivated the venom of cobra, rattlesnake and daboia is a good example. Macht[1] inactivated the toxins of pernicious anemia in human blood serum by short exposure to ultraviolet rays. Schubert[11] gives a report on work with tetanus toxin, and Hausmann, Neumann and Schubert[12] have a published report on work done with tuberculin.

The experimental work *in vivo* presents more difficulty in drawing accurate conclusions. In blood irradiation therapy, however, clinical evidence of inactivation of toxins within the patient is readily discernible. In cases of severe infections that recover, a marked diminution of toxic symptoms is noticed within twelve to forty-eight hours after treatment. Malaise, severe headache, nausea, mental confusion, chills, fever and other toxic symptoms are generally relieved. The temperature usually drops, as does the white cell count.

The blood sedimentation rate is generally decreased markedly. In the occasional case in which the temperature remains high there will be observed a marked reduction in toxic symptoms. If this condition is accompanied by a reduction of the pulse rate to normal, it usually indicates some localized infection or abscess. However, the patient's condition has improved from the critical stage to a noncritical one. The reduction of toxic symptoms of the patient is one of the most important guides in determining if the treatment should be repeated.

The destruction or attenuation of bacteria is shown in the accompanying charts. The time of exposure necessary to kill different bacteria with ultraviolet rays under controlled conditions of wave-length, temperature and intensity has been found to vary. It has also been found that exposure insufficient to destroy bacteria in one medium may be sufficient to destroy them in a different medium. When a small part of the total infected blood stream is irradiated for a period of time less than required to kill bacteria in a different medium, a complete attenuation or destruction of bacteria is generally achieved. The blood specimens that developed profuse growth in cultures (e.g., Streptococcus hemolyticus) before irradiation showed no such growth within twenty-four to seventy-two hours after the first or second irradiation. It must be noted, however, that with certain pathological conditions more than two treatments may be necessary to achieve this result.

The bactericidal properties of ultraviolet energy are partially explained by the minuteness and by the chemical structure of bacteria—certain bacteria are destroyed by an amount of irradiation which merely stimulates normal body cells. There are two causes for this; first, body tissue cells are immense compared to bacteria cells, so that we might expect and actually do get different results when irradiation impinges upon them; second, there occur rather freely in certain bacteria two photosensitive amino acids—phenylalanin and tyrosin—which occur but slightly in body cells. These acids cause greater absorption of ultraviolet by the bacteria which brings about coagulative

or destructive changes in them, without lowering resistance of normal body cells which are not as photosensitive.

The Rockefeller Institute recently announced that they have found a more effective method of preparing vaccines, by using ultraviolet rays instead of heat to render the viruses nonvirulent. They are using this method to prepare *in vitro* vaccines for influenza and rabies. In hemo-irradiation on patients with blood stream infection, only a small portion of the patient's total volume of blood is treated. There is some reason to believe that by destroying the bacteria in the treated portion of the blood, an autogenous vaccine is produced which, coupled with the action of induced secondary irradiation causes destruction of the bacteria in the blood stream.

Induced secondary irradiation is a known physical phenomenon and easily demonstrated with human blood irradiated with ultraviolet. Hemoglobin absorbs radiation over a wide range of wave-lengths; in the ultraviolet region of the spectrum it absorbs strongly. Secondary irradiation can be readily demonstrated by placing irradiated blood in a thin-walled quartz vessel and setting it on an ultraviolet-sensitive film; the film will be fogged. This secondary irradiation probably accounts for some of the cumulative effects and remote results of hemo-irradiation. It can be shown clinically that certain effects which are observed shortly after treatment are increased for some period of time: a reduction of toxic manifestations in certain cases, a feeling of warmth in others, and a definite peripheral vasodilation in almost all.

Studies in oxygen absorption values of blood after hemo-irradiation were recently made by Miley.[5] Increased oxygen combining power of the blood is readily observed clinically. Patients who are cyanotic from the administration of sulfanilamide or other drugs, or from some pathological condition, usually have their cyanosis disappear within a few minutes after treatment. In pneumonia patients this is particularly striking. Extreme cyanosis generally disappears within a few minutes.

We present here seven case histories; four histories of patients with hemolytic streptococcic septicemia, two histories of staphylococcic septicemia, and one history of colon bacillus septicemia. The colon bacillus septicemia was not treated by the writer but was the patient of another physician who used this treatment.

The writer was called in on two other cases of hemolytic streptococcic septicemia, but the patients were moribund and treatment did not help.

Five cases of Streptococcus viridans septicemia have been given hemo-irradiation. Three of these patients had advanced endocarditis when first treated and were only helped temporarily. The fourth had no detectable heart lesion and treatment was given in the early stages of the infection. The patient was irradiated in 1936 and returned to work six weeks later. He was last seen in 1941 and there has been no return of symptoms since 1936; he is apparently completely well today. The fifth patient had a well developed Streptococcus viridans septicemia, but also had no detectable heart involvement in 1938 when he was treated. He is still an invalid in 1941, invalidism being due to complicating influenzal meningitis and chest involvement. The patient apparently is progressing to recovery.

CASE REPORTS

Case 1. No. 30146. Mrs. G. G., thirty-seven years of age, was admitted to Virginia Mason Hospital, Seattle, Washington, on August 14, 1933, and gave the following history: Her last menstruation occurred on August 2. The usual signs of pregnancy were evident until September 30 when the normal menstrual flow started and continued until October 13 when severe hemorrhage occurred and she passed some membranes.

Physical examination revealed a firm but not tender uterus almost to the umbilicus; no fetal heart tones could be heard. There was a moderate amount of vaginal flow; temperature was 99°F., pulse 84, respirations 18. The tem-

perature remained practically normal until nine days after admission. The patient did not respond to pituitrin and hot packs.

ran a septic temperature despite transfusion, intravenous mercurachrome and iodine injections into the uterus, and she was critically ill.

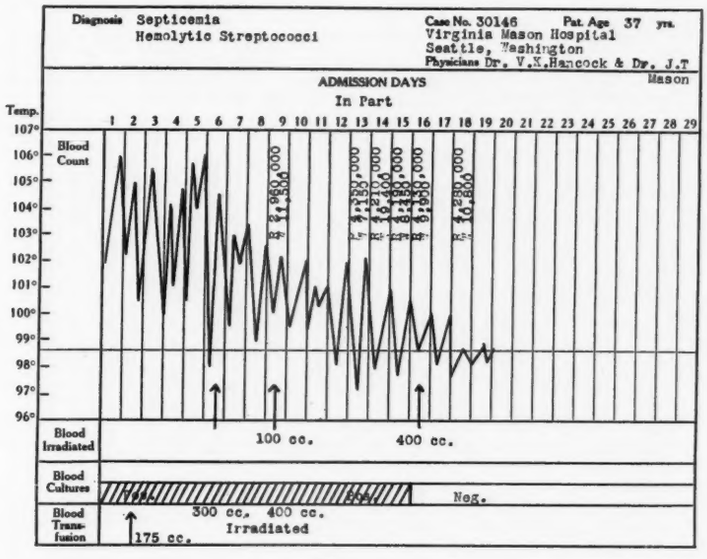

FIG. 1.

On October 24, dilatation of the cervix and induction of labor were advised. A small rectal tube was inserted at 10 A.M. and expelled in the afternoon with a small piece of placenta tissue the size of three fingers. On the following day a septic temperature began. Two days later a Bougie bag was inserted which was expelled later, producing but little dilatation. On October 28, the patient's temperature was 103.6°F., pulse 150 and respirations 20. Under ether anesthesia the cervix was dilated and it was found filled with multiple fibroids; there was a posterior cervical tear sufficient to insert one finger. With a sponge forceps in the uterus a pedunculated fibroid was lifted out and it was determined that the canal of the uterus was very torturous and filled with projecting fibroids. The cervical tear was repaired and two ounces of iodine were injected into the uterus at 5:40 P.M.

On October 29, the patient's temperature was 97.6°F., pulse 84 at 4 A.M. Temperatures averaged 105° to 106°F. for six days which was brought down each day by iodine injections into the uterus. A forty-eight hour blood culture showed Gram-positive bacteria, a few in chains, resembling streptococcus.

On November 8, this patient was irradiated and Figure 1 shows the course of this patient toward recovery once irradiation was started. From October 27 to November 8 this patient

On November 9, one day after the first hemo-irraditiona, temperature peaks fell to 103°F. During the next three days peaks were 102° then 101°F. until November 20. After that the temperature fell to 99°F. where it remained until December 6. Peaks climbed again to 103°F., when menstruation started, and continued at that point until December 28 when it dropped to normal.

This patient gets considerable absorption from the uterus but blood cultures remain negative. It is planned to do a hysterectomy at the opportune time.

CASE II. No. 53842. Mrs. B. W. was seen at her home September 28, 1938, suffering from typical renal colic pain in the left kidney and course of the left ureter. One-quarter gr. of morphine was administered which was repeated an hour and a half later. The pain subsided until 10:00 A.M. the following morning when it returned. The patient's temperature was 102.2°F and she was sent to the hospital. That night she had a chill and vomited.

There was swelling, extreme pain and tenderness around the left kidney. On the sixth day of admission, 25 gr. of sulfanilamide were given followed by 50 gr. on the seventh day. Due to added toxicity, a decrease in red cells and no apparent response, this treatment was discontinued. She had a chill each night until Octo-

ber 11 when the temperature rose to 108.4°F. (axilla).

At 3:00 P.M. the patient was irradiated and

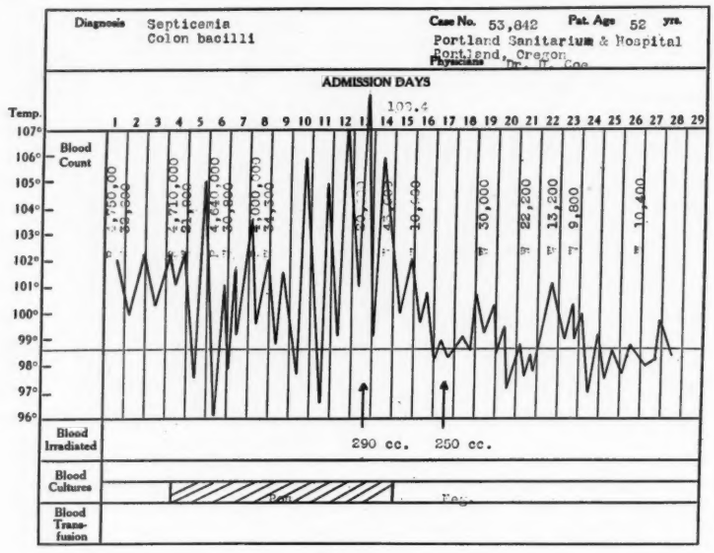

FIG. 2.

the temperature dropped steadily to 102°F. on October 13. Another irradiation was given on October 15 and the patient's temperature gradually returned to normal, averaging 99°F. She was discharged on October 26 and made a rapid and uneventful recovery. When last seen on March 1, 1940, the patient was enjoying normal health. (Fig. 2.)

The final diagnosis was pyelitis with colon bacilli septicemia.

CASE III. No. 10081. E. O'B., a female, fifteen years of age was admitted to Columbus Hospital, Seattle, Washington, on July 26, 1935, with a temperature of 103°F., and pulse 120.

Two weeks before admission she had a nasal discharge following diving and swimming. Five days before admission she had visited a doctor and upon returning home noticed a swelling of both jaw and neck on the right side. Four days later the same swelling appeared on the left side of the neck and jaw. The patient vomited after taking pills; she had chills, fever, malaise and general weakness. The pain in the back of the head recurred and there was some painful movement in fingers and wrists with swelling.

Physical examination revealed the posterior side of the pharynx well injected with dilation of the veins. There was a questionable piece of tonsil tissue present in the right fossa. The right cervical glands were swollen, tender, hot, red and painful. The left cervical gland was less enlarged but some painful posterior auricular nodules were present. The right wrist was somewhat painful and the left wrist was less painful. There was some evidence of heat and swelling in both wrists. The heart revealed a definite pulmonic murmur.

The patient had a septic temperature for twenty-one days ranging from 96° to 106.8°F. On the twenty-second day after admission this patient's blood was irradiated and from then on she progressed to an uneventful recovery. (Fig. 3.)

The diagnosis in this case was infectious pharyngitis with cervical adenitis; hemolytic streptococcic scepticemia.

CASE IV. No. 11252. J. D., a male, twenty-two years of age was admitted to Columbus Hospital, Seattle, Washington, on January 6, 1936, with a temperature of 102°F. and a pulse of 70.

He had been hit by a car on December 26, 1935, and was found by the side of the road and taken to an Army Post Hospital where ten stitches were placed in a scalp wound on the right side. He stayed at that hospital overnight and was treated later at the doctor's office. The stitches were removed about January 1. He claimed that infection had set in and the scalp wound had become swollen with resultant closure of the right eye. Headaches persisted since the accident but no *x*-rays had been taken. Continual hot packs had reduced the swelling which became localized behind his right ear and

beneath the right cheek. On the day of admission he noticed the presence of a sore throat with tenderness over the right mastoid region. There was no complaint of pain in the ear.

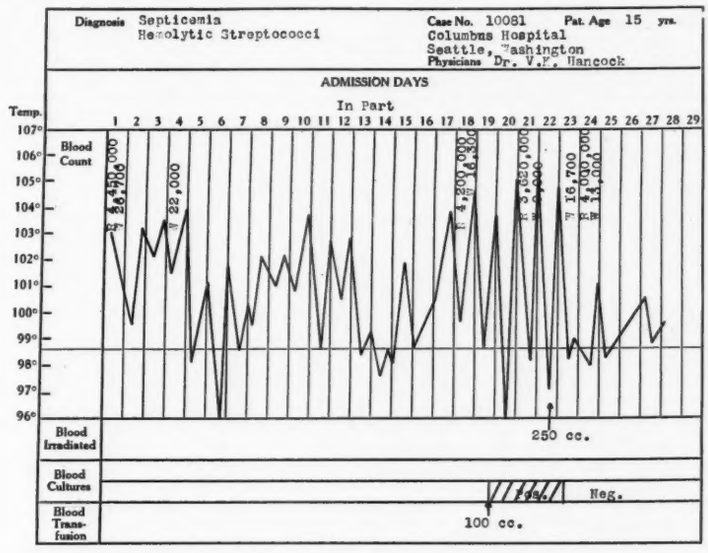

Fig. 3.

Physical examination revealed the patient to be fairly comfortable but the head was held in a fixed position. There was some fever and swelling of the right cervical glands. The scalp wound was indurated with some exudation.

The diagnosis in this case was cellulitis of the scalp wound and hemolytic streptococcic septicemia.

Case v. No. 38434. R. F. R., a female, twenty-one years of age, was admitted to

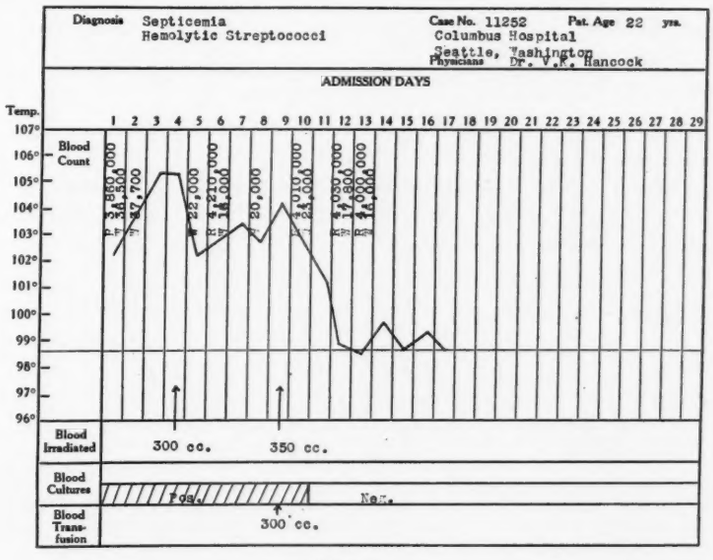

Fig. 4.

The genitourinary and gastrointestinal examinations were negative. The blood cultures were returned positive for hemolytic streptococcus.

This patient was given two blood irradiations and the cultures became negative within twenty-four hours after the second irradiation. From then on his recovery was uneventful. (Fig. 4.)

Virginia Mason Hospital, Seattle, Washington, on January 23, 1935, with a temperature of 102.2°F. She gave the history of accidental miscarriage twelve days previously of a two month pregnancy. There had been considerable

hemorrhage. The mass was removed from the cervix with forceps and irrigation was instituted. Three days later the patient had a chill, fever and bloody sputum.

The diagnosis in this case was postabortional septicemia, hemolytic streptococci and bacteriemia.

Case vi. No. 33902. C. H. G., a male,

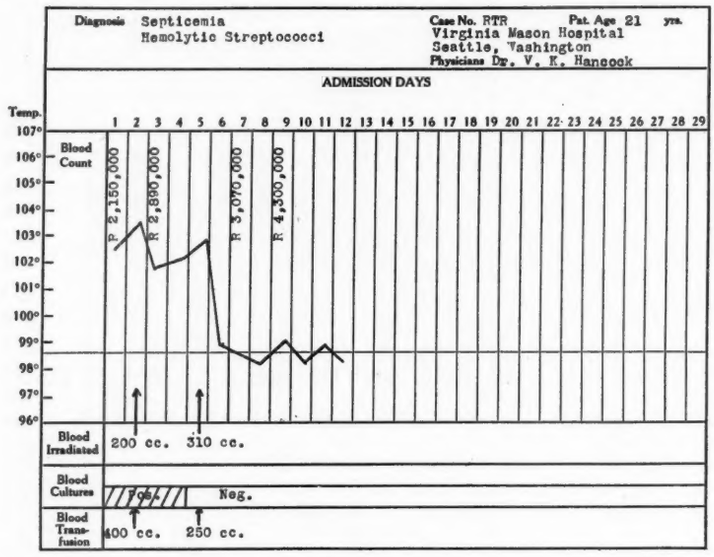

Fig. 5.

The physical examination revealed the patient to be very ill with a septic temperature of 103.6°F. Her pulse was rapid, the chest was negative and there was tenderness in the lower portion of the abdomen. Blood cultures were positive for hemolytic streptococci. Two irradiations were given this patient and her temperature dropped to 98.8°F. twenty-four hours after the second irradiation. From this point the patient had an uneventful recovery. (Fig. 5.)

forty-two years of age, was admitted to Virginia Mason Hospital, Seattle, Washington, on January 14, 1935, with a history of severe pain in the right leg. On January 22, there was swelling, local tenderness and signs of inflammation of the lower part of the leg at the area of injection. There were no definite signs of localization. He had a septic temperature of 104°F. There was not much pain, no fluctuation and no indication for drainage.

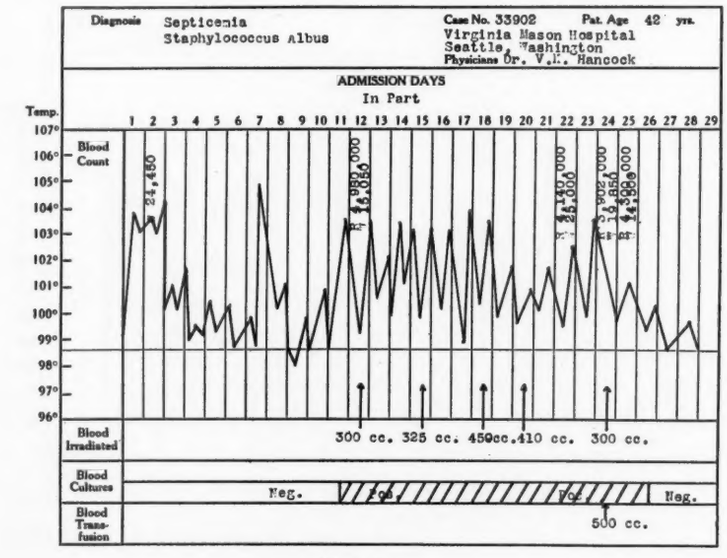

Fig. 6.

On January 28, incision and drainage of abscess over the medial side of the knee joint were carried out. His temperature at that time was 104.8°F. On February 1, it was decided to carry out further drainage. An incision was made in the midthigh and some pus was encountered. Another incision was made just below the knee anteriorly and through-and-through penrose drains were inserted.

On February 4, the patient was definitely improved. The induration of the thigh had decreased, there was no fluctuation and he suffered very little pain. On that day the right inguinal lymph glands were enlarged, reddened, indurated and painful. On February 5, the glands in the right groin were swollen, painful and inflamed. Induration in the upper part of the thigh had decreased and the wound drained slightly. On this day a blood culture showed positive staphylococci (loaded).

On February 6, this patient was irradiated and this procedure was carried out a number of times until February 14. When the blood culture was taken on February 17 it was found to be negative. The patient was discharged on February 20 with the final diagnosis of varicose ulcer with infected right leg complicated by phlebitis of the right leg and thigh and staphylococcic septicemia. The patient recovered completely from septicemia and convalesced for six weeks before becoming actively engaged at his trade. (Fig. 6.)

Case vii. No. 4126. C. C., a female, nine years of age, was admitted to the Maynard Hospital, Seattle, Washington, on June 3, 1934, with the following history: temperature, 104.2°F. There had been pain in the left leg four days previously which was generalized at first and later localized in the left hip. There was no gross swelling in this area and no paralysis of the leg but the patient experienced a great deal of pain when moved.

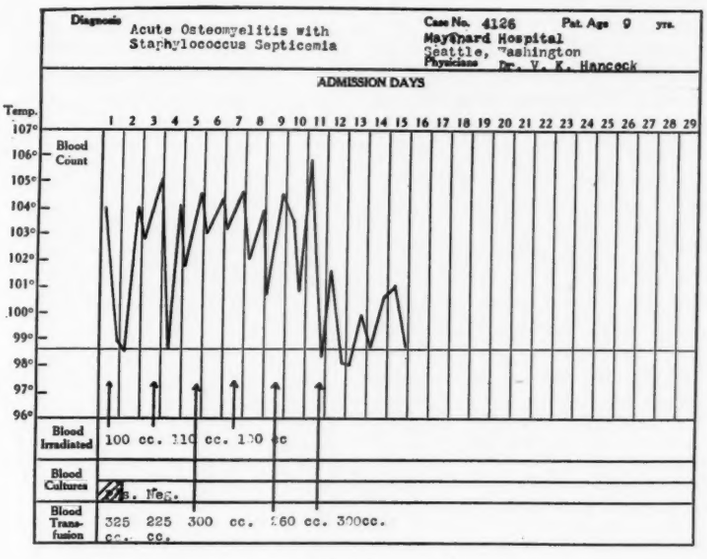

Fig. 7.

The child appeared very ill and toxic; the tonsils were enlarged and reddened and the throat could not be well visualized. There was some thick mucopurulent discharged in the throat and marked tenderness and pain in the right thigh.

On June 3, *x*-ray was negative but clinical findings indicated acute osteomyelitis. A window was made in the left femur and irradiation was carried out. Blood culture was positive for staphylococcus. On the following day a window was made in the medial inferior end of the right tibia. A blood culture at that time was negative. On June 5, an *x*-ray revealed slight bronchitis or an early stage of bronchopneumonia. A second irradiation was carried out. On June 6, an opening was made into the left lateral posterior inferior femur extending into cancellous bone.

This patient had been given a number of irradiations plus donor blood transfusions. The diagnosis was acute osteomyelitis, bronchopneumonia and staphylococcic septicemia. This child had had three operations in four days. Two days after the first irradiation the blood stream was negative. She was discharged

in seventeen days and has followed the usual postoperative care and progress. (Fig. 7.)

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Dental operations involving the palate are best done with the patient under block anesthesia or infiltration anesthesia although the intratracheal method of administering an anesthetic agent by inhalation often may be used to advantage.

PRIMARY BRAIN TUMOR*

FOLLOW-UP STUDY OF 179 CASES

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DR. HARVEY CUSHING stated in the introduction to his classical monograph[1] on intracranial tumors that "precise information in regard to what has happened to the survivors is more important than the mere statistical enumeration of the dead and living." This suggestion that the time had arrived for an assay of the value of surgery in the treatment of cerebral neoplasms has not been generally followed, although the notable contribution of Van Wagenen[2] disclosed most important information. Van Wagenen's study revealed for the first time not only the mortality statistics but a careful appraisal of the end results in terms of a useful and happy postoperative existence. The technical methods for the surgical attack have now been perfected. What we need to know is, what may the individual patient expect and hope for after the ordeal, and can prognosis be more definite?

With these thoughts in mind, the 179 cases of primary brain tumor seen at the Peter Bent Brigham Hospital between July 1, 1932, and June 1, 1941, have been carefully analyzed, and the information gathered from this study as a check-up on a representative group of brain tumor cases is presented here. No new methods of therapy are suggested, but this follow-up has laid emphasis on the end results as viewed by lay people whose desire for prognosis concerns the usefulness of the individual after therapy as well as the simple mortality rates. All patients except seven responded to follow-up letters or visited the follow-up clinic. No patients seen prior to July 1, 1932, were included since they are numbered in Dr. Cushing's series and have been commented upon by others.[2–5] Of the 179 cases, 150 were verified by histologic study, and twenty-nine by ventriculography or pneumo-encephalography.

On the whole, the incidence of the various types of brain tumors in this series parallels that found by Cushing[1] in his report of 2,000 cases. (Table 1.) About one-half of our cases were gliomas, with pituitary tumors and meningiomas next in frequency. The unclassified brain tumors, that is, those which were not verified histologically, made up 16.2 per cent of the total. The meningiomas, acoustic neuromas, pituitary adenomas, cystic gliomas, blood vessel tumors, and unclassified cysts, those types considered favorable by Horrax,[6] made up less than one-third of our series, whereas in the cases reported by Horrax[6] 54.5 per cent fell in this favorable group. This difference in favorable cases is

TABLE 1

Type of Brain Tumor	No.	No.	Per Cent
Gliomas (varia)	..	89	49.7
Pituitary tumors	..	25	13.9
Chromophobe	17		
Acidophil	2		
Basophil	1		
Craniopharyngioma	5		
Meningiomas	..	19	10.6
Acoustic neuromas	..	7	3.9
Blood vessel tumors	..	4	2.2
Neuroblastomas	..	3	1.7
Lipoma	..	1	0.6
Chordoma	..	1	0.6
Melanosarcoma	..	1	0.6
Unclassified brain tumors	..	29	16.2
Total	..	179	100.0

* From the Surgical Clinic of the Peter Bent Brigham Hospital, Boston.

only the expected variation occurring in separate clinics and is largely a matter of fate.

A total of 251 operations, including burr holes, subtemporal decompressions, and osteoplastic bone flaps, was performed upon 166 patients. (Table II.) The case tion and whom we have been able to follow, seventy-two are dead. Two lived for over seven years, but the majority of these patients died within one year of operation, in each instance the time of operation being the time of the initial diagnosis. When the gliomas are excluded, it should

TABLE II

	No. of Patients	Patients Operated Upon	No. of Operations	Postoperative Deaths	Case Mortality, Per Cent	Operative Mortality, Per Cent
Gliomas (varia)	89	87	141	27	31.0	19.1
Pituitary tumors	25	17	19	4	23.5	21.0
Meningiomas	19	19	27	5	26.3	18.5
Acoustic neuromas	7	7	10	1	14.2	10.0
Blood vessel tumors	4	4	6	0	0.0	0.0
Neuroblastomas	3	3	5	0	0.0	0.0
Lipoma	1	1	2	1	100.0	50.0
Chordoma	1	1	2	1	100.0	50.0
Melanosarcoma	1	1	1	0	0.0	0.0
Unclassified brain tumors	29	26	38	2	7.7	5.3
Totals	179	166	251	41	24.7	16.3

mortality was 24.7 per cent for the entire group. For the gliomas the case mortality was 31 per cent; for the meningiomas, 26.3 per cent; and for the pituitary tumors, 23.5 per cent. The total operative mortality was 16.3 per cent, being 21 per cent for pituitary tumors; 19.1 per cent for gliomas; and 18.5 per cent for meningiomas. These figures are high and demonstrate that a serious mortality is still to be expected following surgery for brain tumor. No attempt has been made to lower these figures by weeding out those who died of complications not directly related to the underlying disease or to the operation. It should be mentioned here that we have abandoned the more radical procedures in the treatment of pituitary adenomas and cerebellar medulloblastoma and are now treating these tumors with *x*-ray irradiation. The results of this form of therapy have been reported elsewhere,[7,8] and are more encouraging than the results following radical surgical treatment.

Of the 131 patients who survived operabe noted that there were comparatively few early deaths among those patients with the more favorable types of brain tumor, and that those suffering from meningiomas or acoustic numeromas had several years of useful life following operation.

The results with the gliomas were the most discouraging, probably due to the fact that there was a high incidence of glioblastoma multiformi in our cases. (Table IV.) Two patients with glioblastoma multiformi survived for more than two years. These two patients were treated by decompression and biopsy, followed by radiation by *x*-ray in the same manner that we are now treating those with cerebellar medulloblastoma. We believe that this method of handling the rapidly growing gliomas will offer patients a more useful life for their remaining days. On the other hand, slow growing gliomas, such as the astrocytomas, can still be treated as focal lesions and an attempt can be made to remove them. Patients with cerebral medulloblastoma do not do well under any type of management;

although two patients are reported alive and well eight years after operation with cerebral medulloblastoma.

However, we believe that by intelligent use of decompression and biopsy followed by radiation therapy a better prognosis may be offered than by radical attempts to remove all of a rapidly growing glioma.

TABLE III

Type of Brain Tumor	Total No. of Patients Dead	Survival Period before Death									
		Postoperative Deaths	1–6 Mos.	6–12 Mos.	1–2 Yrs.	2–3 Yrs.	3–4 Yrs.	4–5 Yrs.	5–6 Yrs.	6–7 Yrs.	7–8 Yrs.
Gliomas (varia)	72	27	20	10	4	3	2	2	1	1	2
Pituitary tumors											
Chromophobe	3	3									
Acidophil	1	..	..	..	..	..	..	1			
Basophil	0										
Craniopharyngioma	2	1	..	..	1						
Meningiomas	11	5	2	1	..	..	1	2			
Acoustic neuromas	3	1	1	..	..	..	1				
Blood vessel tumors	1	..	1								
Neuroblastomas	2	..	1	1							
Lipoma	1	1									
Chordoma	1	1									
Melanosarcoma	1	..	..	..	1						
Unclassified brain tumors	15	2	5	4	4						
Totals	113	41	30	16	10	3	4	5	1	1	2

Gliomas, the most common brain tumors, include the most malignant intracracranial tumors as well as the most benign. In any large series of brain tumors a considerable mortality will be encountered in the gliomas, and aside from radiation therapy in addition to surgery there is nothing to offer.

Fifty-nine (32.9 per cent) of the 179 patients are still alive. Careful follow-up studies of recent date were obtained upon these survivors. (Table v.) A precise study of the condition of these patients shows

TABLE IV

Type of Glioma	Total No. of Patients Dead	Survival Period before Death									
		Postoperative Deaths	1–6 Mos.	6–12 Mos.	1–2 Yrs.	2–3 Yrs.	3–4 Yrs.	4–5 Yrs.	5–6 Yrs.	6–7 Yrs.	7–8 Yrs.
Glioblastoma multiformi	35	16	11	5	1	1	1				
Cerebellar medulloblastoma	11	1	2	1	1	2	1	1	1	..	1
Cerebral medulloblastoma	3	2	..	1							
Astrocytoma	17	5	7	2	2	..	..	..	..	1	
Oligodendroglioma	4	3	..	..	..	..	..	1			
Ependymoma	2	0	..	1	..	..	..	..	..	..	1
Totals	72	27	20	10	4	3	2	2	1	1	2

that eighteen (30.5 per cent) suffer serious handicaps or are so badly crippled that they cannot lead useful lives. This means that 30.5 per cent of the survivors present major problems to their families for their care, and except among the well-to-do, this is a great burden. However, lest it be said that pessimism is paramount, 41 (69.5 per cent) of the surviving patients are leading useful lives, although to be sure most of these survivors fall into the class of so-called favorable brain tumors. This parallels Horrax's figure of 70 per cent useful survivals in a larger series of favorable brain tumors.

It must be pointed out that in Table v there are ten patients living less than one year after operation or radiation therapy. It is not intended that these cases should give a false idea of survival, for some of them, especially among the gliomas, may not survive another six months or one year. However, as in the rest of this report, these tables are included to give a candid analysis of a group of intracranial tumors, both dead and alive at the present time.

COMMENT

As stated in this report, little attention has been directed toward the end results following operation for brain tumor. Most reports have dwelt upon mortality statistics, operative technic, and more recently upon favorable types of brain tumors. There are, however, in every group of patients with brain tumor who survive operation, a number who are so handicapped or crippled that they are completely dependent upon others. It is not in apology for those handicapped that this report has been made, but rather it has been our purpose to point out that these patients do exist. The cause of these handicaps is, of course, due to the underlying nature of brain tumors, but may occasionally be due to well intended but ill advised attempts at surgical removal of the lesion. It is difficult to analyze just when surgery

TABLE V

Type of Brain Tumor	Total No. of Patients Alive	Survival Period of Patients Still Alive*									
		1–6 Mos.	6–12 Mos.	1–2 Yrs.	2–3 Yrs.	3–4 Yrs.	4–5 Yrs.	5–6 Yrs.	6–7 Yrs.	7–8 Yrs.	Number Crippled
Glioblastoma multiformi	4	3	1	..	..	..	..	..	..	..	2
Cerebellar medulloblastoma	2	..	..	..	1	..	..	..	1	..	2
Cerebral medulloblastoma	2	..	..	..	..	..	..	..	..	2	0
Astrocytoma	5	..	..	2	..	..	1	..	..	2	2
Oligodendroglioma	2	..	..	2	..	..	..	..	..	..	1
Ependymoma	0										
Pituitary tumors: chromophobe	13	1	1	..	..	1	1	2	2	5	2
Acidophil	1	..	..	..	..	..	..	..	..	1	
Basophil	1	..	..	..	..	..	..	..	1	..	1
Craniopharyngioma	3	..	..	1	..	..	..	1	1	..	1
Meningioma	8	..	..	..	1	2	1	..	3	1	0
Acoustic neuroma	4	..	..	..	1	..	1	2	..	..	1
Blood vessel tumors	2	..	..	..	..	2	..	..	..	..	1
Neuroblastoma	1	..	..	1	..	..	..	..	..	..	0
Lipoma	0										
Chordoma	0										
Melanosarcoma	0										
Unclassified brain tumors	11	3	1	..	2	1	1	..	1	2	5
Totals	59	7	3	6	5	6	5	5	9	13	18

* No follow-up obtainable upon seven patients, excluded from this group.

has been carried too far. We believe that brave attempts to excise irremovable brain tumors should be abandoned for decompression and biopsy followed by radiation therapy. This is not a defeatist attitude, because we agree with Sachs[10] and others that an intracranial neoplasm should be regarded as a focal disease and as such treated by removal. Nevertheless, removal in many instances is not feasible, and much damage may be done in the surrounding areas while the natural course of the tumor is unaffected or even accelerated.

It may be stated fairly that in certain favorable types of brain tumor a good prognosis can be offered the patient. However, even in these instances there is still a relatively high operative mortality, and misconceptions may easily arise concerning the prognosis unless the entire picture is kept in mind, especially among those surgeons who deal only occasionally with brain tumors.

SUMMARY AND CONCLUSIONS

1. One hundred seventy-nine cases of primary brain tumor seen at the Peter Bent Brigham Hospital, Boston, between 1932 and 1941 are reviewed.

2. The gross case mortality was 24.7 per cent and the gross operative mortality was 16.3 per cent.

3. Seventy-two patients survived from a few months to eight years, but the majority lived less than two years.

4. Fifty-nine (32.9 per cent) of the total series are alive at the present time.

5. Eighteen (30.5 per cent) of the living patients are seriously crippled, while the remaining 41 (69.5 per cent) are leading normal lives.

6. Surgery upon brain tumors is still associated with a high mortality and a poor prognosis except for tumors which can be removed locally or which are sensitive to radiation therapy.

7. In giving prognosis, the surgeon must keep in mind both the pathological types of brain tumor and the possible crippling due to neighborhood injury if he is to give a fair appraisal.

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A COMPARATIVE STUDY OF LOCAL BURN TREATMENTS*

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FROM October, 1939, to date we have made a comparative study of four different local preparations for burns, choosing what we believed to be the two best "leatherizing" agents and the two best "nonleatherizing" agents. Although realizing that in major burns the topical application is of decidedly secondary importance to correct principles of treatment, such as asepsis, plasma therapy, nursing care, early skin grafting, etc., we wished to determine which agent, if any, proved the most efficient for use in a large charity hospital with inadequate nursing care and lacking in ideal facilities for treating burns. Such a comparative study seemed the more important since the great majority of reports in the literature upon the local treatment of burns deal with one favorite routine and lack any sort of control.

Since various writers differ somewhat in their gradation of the depth of burns, it is to be understood that in this paper "third degree" connotes full thickness destruction of the skin and its appendages. "Second degree," indicate by blister formation, is of intermediate depth between first degree erythema and third degree.

The present series consists of 199 burns in 192 hospitalized patients. Seven bilaterally similar burns were dressed with a different agent on either side. One hundred patients were treated with "Foille," fifty-four with tannic acid or tannic acid and silver nitrate, thirty with sulfadiazine and eleven with cod liver oil. Several additional patients were excluded from this series because they left too early for an evaluation of their treatment, and four patients with 80, 85, 85 and 100 per cent of body surface involvement were excluded as moribund. Practically all the cases in this series were followed closely by the writer from start to final healing.

METHOD OF TREATMENT

Measures Common to All. All burns, irrespective of their therapeutic group, received as nearly as possible the same general treatment. Unfortunately, the plasma given was seldom the calculated ideal and at times it was grossly insufficient, due to the inadequate supply in the blood bank.

All burns, with the exception of a few desperate cases, in which débridement was omitted, received the same initial local treatment, namely, heavy morphine analgesia and a fairly thorough débridement in the treatment room, employing white soap and sterile water, sterile gloves and instruments. In all more recent cases the attendants have masked.

The late management of third degree burns presented one common objective regardless of the local treatment used, namely, the early-as-possible removal of sloughing corium. About the end of the second week, when the necrotic corium began to separate, periodic tub baths or sterile saline compresses were instituted for mechanical cleansing, and from time to time all detachable corium (and eschar, if present) was gently dissected away with sterile instruments. Foille and cod liver oil dressings were continued on their respective burns right up until time for skin grafting. However, as soon as an appreciable amount of eschar had been removed from the leatherized burns, cod liver oil dressings were applied to the tanned burns and to a few of the sulfadiazine-sprayed burns. The majority of the latter were dressed with sulfadiazine or sulfanilamide ointment.

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All granulating surfaces were covered with Reverdin skin grafts as soon as the last of the necrotic corium was removed and, if possible, before the granulations became well developed.

DISCUSSION OF AGENTS USED

*Foille** is a thick, soapy, water-in-oil emulsion of mildly antiseptic value. Its use in the treatment of burns has been reported by Terrel,[1] Noland,[2] Galt,[3] Hamilton[4,5] and others. It contains:

1. A base of corn oil	
2. Sulfhydryl radical	traces
3. Calcium thiosulfate	0.03%
4. Sulfur	0.17%
5. Calcium oleate	0.36%
6. Oxyquinoline base	0.18%
7. Benzocaine	1.26%
8. Iodides (calcium and potassium)	0.40%
9. Phenol	approx. 1.96%

When applied locally with a spray gun or camel's hair brush, Foille at first appears as a thick, transparent film, but slowly it forms with protein exudates a soft, brownish curdy precipitate. This is easily removed by soaking or sponging. The Foille routine has been described elsewhere.[4,5] Recently, we have begun to apply to the deeper and more extensive lesions an inner layer of several thicknesses of Foille-saturated gauze, and over this a thick, sterile compression dressing of gauze and cellucotton, the whole to be left undisturbed for ten to fourteen days. (Fig. 1.) Allen and Koch[6] and Siler[7] have emphasized the fact that compression dressings reduce the exudation of plasma into the burned area. After the removal of this initial compression dressing, the burn is kept constantly moistened with the agent and left exposed to the air beneath a cradle. We have treated a few of our most recent burns with a modification of Foille, in which the oxyquinoline has been replaced by 1.5 per cent sulfathiazole. This, combined with the initial compression dressing, appears promising.

Fig. 1. Illustrating a compression Foille dressing upon an extensive second degree burn of the left thigh and leg.

The detergent quality of Foille offers important possibilities in modern oil-stained warfare. It will readily dissolve grease and oil as shown in Figure 2, and in burns thus contaminated the patient need not be submitted to the degree of cleansing usually required before the application of one of the other agents. The Foille dressing will at the same time protect the burn and remove the remaining oil.

Cod Liver Oil or Ointment. The local application of this vitamin oil, introduced originally by Lohr,[8,9] has recently been used by Hardin,[10] Steel[11] and others. We have employed both the oil and the vitamin ointment with petrolatum base and have followed a routine nearly identical with that used for Foille. Thus far we

* Dr. David E. Levin, technical director of the Carbisulphoil Company (producers of Foille) states that the original ingredients: corn oil, calcium hydroxide, sulfur, phenol and iodine are first emulsified together and later the oxyquinoline and benzocaine are added. The tabulation above is the chemical analysis of the finished product rather than a "shotgun prescription."

have confined its use to less severe, smaller burns.

Tannic Acid with and without Silver Nitrate. Davidson's[12] tannic acid treatment for burns is doubtless still the most popular of all methods and needs no further description. In many of the cases in this group we used the combined tannic acid and silver nitrate method of Bettman[13] to hasten eschar formation. In the larger burns, the initial débridement was carried out with the patient totally immersed in a tannic acid bath, as described by Wells.[14] The warm solution greatly relieved suffering and, at the same time, diminished the tendency toward shock.

*Sulfadiazine.** The application of 3 per cent sulfadiazine in 8 per cent triethanolamine to burns was introduced by Pickrell[15] in 1941. Adams and Crawford[16] also used this sulfonamide on fifty burns. We followed Pickrell's technic with the exception of not omitting the initial soap and water cleansing. Usually about four days were required to complete eschar formation. Folds subject to masceration and surfaces of necessity lain upon, frequently failed to form an eschar. Also, the sulfadiazine eschar was quite prone to crack and allow exudation and crustation. The sulfadiazine blood level reached its peak in the majority of our cases within twenty-four hours, a few between the thirty-sixth and forty-eighth hour. One patient with 35 per cent of the body surface involved reached a peak of 12.8 mg. per cent in thirty-six hours; another with 28 per cent of surface involved reached a peak of 32.5 mg per cent in thirty-six hours; and a third with 65 per cent of her body surface burned showed a level of 25 mg. per cent in twenty-four hours. These figures show the need of following closely the blood levels of the drug in extensive burns.

Recently, we have begun to use a 1.5 per cent solution of sulfadiazine in triethanolamine to which 1.67 per cent methocel was added to make a faster drying film. With this preparation an eschar forms in about thirty hours, as compared to the ninety-six hours required by the original solution. However, the eschar itself is a cellodion-like film that adheres rather poorly and cracks and melts in places. It is, therefore, less satisfactory, we believe, than the original.

A B

FIG. 2. A, feet covered with heavy, sticky oil; B, the same feet. The right foot has been cleaned for eighty seconds with Foille and the left for fifty-five seconds with gasoline.

* Supplied us by the Lederle Laboratories.

MORTALITY AND SURVIVAL

Thirty-eight of the 192 patients in this series died, a mortality of 19.8 per cent. Some slight excuse can be made for this appalling figure. The nursing care was inadequate, there were no facilities for

TABLE I

ANALYSIS OF FATAL CASES

Name	Age	Per Cent Body Surface Burned				Agent	Time of Death (d. day) (h. hour)	Inadequacy of Plasma Therapy†	Remarks
		1st	2nd	3rd	Total				
H. L.	42	0	13	5	18	Foille	9th d.	Adequate	Cause of death uncertain
S. B.	24	5	17	17	39	"	16th d.	Marked	Cause of death toxemia and pneumonia
M. M.*	44	0	45	0	45	"	4th d.	Marked	Advanced hepatic cirrhosis. Smoke inhalation
W. H.	4	4	9	13	26	"	26th d.	Adequate	Overwhelming sepsis
B. H.	7 mo.	0	25	3	28	"	14th h.	Moderate	Death due to burn shock
C. D.*	62	0	4	6	10	"	44th d.	Adequate	Marked obesity. Diabetes. Arteriosclerosis
C. J.	71	1	5	2	8	"	17th d.	Adequate	Arteriosclerosis and hypertension
E. D.	72	0	2	9	11	"	55th d.	Adequate	Arteriosclerosis. Burn 4 days old and grossly infected at entry
W. P.	52	0	10	20	30	"	8th d.	Moderate	Became delirious. Temp. up to 105°F.
J. C.	34	0	9	7	16	"	41st d.	Adequate	Chronic alcoholism. Uremia; pneumonia
E. I.*	24	0	12	2	14	"	36th h.	Moderate	Cause of death uncertain
R. U.	4	10	25	20	55	"	4th d.	Adequate	Cause of death burn shock; pneumonia
E. W.	67	0	20	20	40	"	2nd d.	Marked	Hypertensive heart disease
T. H.	63	0	5	10	15	"	22nd d.	Adequate	Hypertensive heart disease; auric. fibrillation
D. M.*	13	0	20	40	60	"	33rd d.	Adequate	Death due to hepatic failure
P. P.*	58	0	3	15	18	"	25th d.	Adequate	Hypertension; arteriosclerosis; cerebral accident
E. J.*	71	0	11	11	22	"	26th h.	Adequate	Arteriosclerotic heart disease
M. H.*	11	0	17	9	26	Foille & Tan	3rd d.	Marked	Death apparently due to burn shock
S. F.*	29	0	9	0	9	"	8th d.	Adequate	Cause of death uncertain. History of pellagra
G. S.*	4 mo.	0	13	2	15	Tan	12th h.	Moderate	Cause of death uncertain. Possibly shock
G. Q.	1	0	16	0	16	"	16th d.	Moderate	Died following hematemasis
M. B.	2	1	56	0	57	"	7th h.	Marked	Death apparently due to burn shock
H. R.	19	3	13	0	16	"	3rd d.	Adequate	Cause of death uncertain
M. F.	65	0	11	0	11	"	21st d.	Adequate	Obesity; burn infected at entry
D. P.	25	2	43	20	65	"	6th d.	Marked	Death due to shock and toxemia
L. B.	61	0	8	0	8	"	27th d.	Adequate	Obesity; death sudden; question of coronary
J. W.	1	0	29	0	29	"	16th h.	Moderate	Sudden death; cause doubtless shock
T. O.	25	0	30	0	30	"	4th d.	Marked	Hematemasis
M. L.	58	0	36	9	45	"	21st h.	Marked	Death due to burn shock
S. H.*	2	4	50	0	54	"	2nd d.	Adequate	Death from shock despite adequate plasma
M. C.	45	0	16	26	42	"	31st d.	Adequate	Obesity; sepsis and exhaustion
E. W.	87	0	13	4	17	Sulfa.	42nd d.	Adequate	Hypertension; senility; pneumonia
E. B.	72	0	8	7	15	"	39th d.	Adequate	Hypertension; arteriosclerosis
G. B.*	22	0	34	30	64	"	4th d.	Marked	Aneuria; blood sulfadiazine level 28.8 mg. %
M. Mc.*	80	0	29	2	31	"	5th d.	Adequate	Arteriosclerosis; smoke inhalation
G. P.	22	2	10	23	35	"	24th d.	Adequate	Became badly infected
C. O.	5	0	11	14	25	"	24th h.	Adequate	Death from shock despite adequate plasma
S. D.	1	2	5	0	7	C.L.O.	3rd d.	Adequate	Fulminating pneumonia

* Autopsied case.

† Expressed as:—"adequate," "moderate" (inadequacy) and "marked" (inadequacy).

isolation and few for special care of burns. As will be seen from the mortality analysis (Table 1) the amount of available plasm and blood was seriously inadequate in ten cases and moderately so in six cases. Six burns involved 50 per cent of total body surface and a number of patients were in the extremes of age or were suffering serious organic disease.

The findings of Dr. A. J. Miller of the Department of Pathology in the 12 autopsied cases are given in Table II. Generalized congestion of viscera, especially of lungs, gut, adrenals and spleen, such as described

TABLE II

ANALYSIS OF FINDINGS IN TWELVE AUTOPSIES

Name	Age	Time of Death	Per Cent Area Involved	Agent	Kidneys	Adrenals	Liver	Other Findings
R. P.	58	25 d.	18	Foille	Marked congestion; slight cloudy swelling	Not remarkable	Slight fat infiltration; moderate acute congestion; marked hemosiderasis	Bronchiectasis and bronchopneumonia; coronary sclerosis
D. M.	13	33 d.	60	"	Moderate congestion; slight cloudy swelling	Moderate congestion	Marked fat infiltration; also vacuolar degeneration of cells; slight early focal necrosis	Small epicardial hemorrhage; slight early bronchopneumonia
C. D.	62	43 d.	10	"	Not remarkable	Marked cortical hyperplasia and focal degeneration	Marked fat infiltration; also vacuolar degeneration of cells; slight early focal necrosis	Patchy myocardial fibrosis; basilor congestion of lungs
E. I.	24	24 h.	14	"	Not remarkable	Focal degeneration and hemorrhage of cortex	Very slight fat infiltration; slight central atrophy	Heart and lungs negative
M. M.	44	96 h.	40	"	Severe cloudy swelling; "toxic nephrosis;" old arteriosclerotic infarcts	Not remarkable	Marked old portal cirrhosis; only slight fat infiltration and no necrosis of regenerated lobules	Tracheobronchitis from smoke inhalation; heart negative
E. J.	71	31 h.	22	"	Severe cloudy swelling; "toxic nephrosis"	Congestion and focal hemorrhage	Slight old portal cirrhosis; slight fat infiltration; little recent damage	Marked pulmonary congestion and edema and early patchy pneumonia; severe myocardial fibrosis
S. F.	29	7 d.	9	Foille and tan.	Arteriosclerotic changes; marked cloudy swelling; "toxic nephrosis"	Congestion; focal lipoidosis of cortex	Marked cloudy swelling of liver cells as from some toxin; no fat infiltration	Lungs and heart not remarkable
M. H.	11	60 h.	26	"	Moderate acute congestion	Moderate congestion and focal hemorrhages	Marked atrophy and early patchy necrosis; very slight fat infiltration; hemosiderosis	Intense pulmonary congestion and edema; heart not remarkable
M. L.	58	32 h.	45	Tan	Not remarkable	Moderate congestion	Marked fat infiltration; early slight focal necrosis	Intense pulmonary congestion and edema; heart not remarkable
G. S.	4 mo.	21 h.	15	"	Moderate congestion; a few red cells in glomerular spaces	Not remarkable	Slight fat infiltration and slight degeneration of cells	Moderate congestion and hemorrhage into pulmonary alveoli; some epicardial and myocardial hemorrhages
S. H.	2	24 h.	50	"	Not remarkable	Intense congestion and focal cortical hemorrhages	Marked hydrops and edema of cells; no fat infiltration or necrosis	Intense congestion and some hemorrhages into pulmonary alveoli; heart not remarkable; marked hyperplasia of thymus and lymphnodes
M. Mc.	76	5 d.	31	Sulfa.	Severe cloudy swelling; "toxic nephrosis;" arteriosclerosis	Not remarkable	Slight chronic passive congestion; marked hemosiderosis; no necrosis of cells	Marked tracheobronchitis from smoke inhalation; myocardial fibrosis

by Moon[17] in animals dying of traumatic shock was found to a varying degree in patients dying in the first three or four days. This was particularly marked in M. H., M. L., G. S., and S. H., who had been grossly undertreated with plasma and blood.

The liver was the organ most frequently and seriously deranged, although not so constantly or specifically as Wilson and co-workers,[18] and McClure[19] found in their autopsies. Fatty infiltration, the commonest finding, occurred both early and late. Varying degrees of cell atrophy and degeneration and one instance of acute hydrops were found. There was no instance of well developed central necrosis nor of eosinophile infiltration. Liver damage was as pronounced in patients treated with Foille as in those treated with tannic acid, which is not in accord with the suspicion[20,21] that the latter is responsible for liver necrosis in burns. In short, our cases reveal no characteristic liver lesion; nor can it be predicted from the severity of the burn, from the application used, or from the time of death, just what the liver will show. Possibly in these few cases the variation in amount of plasma therapy has distorted the picture as iodine therapy has done in the case of hyperplastic goiter.

The adrenals showed variations in degree of congestion up to the point of scattered hemorrhages into the inner cortex. Usually the more marked reaction accompanied the severe burns with early termination. Lipoid changes were also found in some of the cortical cells. The kidneys for the most part manifested differing degrees of congestion. Three patients, two treated with Foille and one with sulfadiazine, showed enough cloudy swelling of the tubules to be called "toxic necrosis." There was marked hyperplasia of the thymus and lymph-nodes in one two-year old baby (S. H.) dying in twenty-four hours. The remaining organs were, on the whole, noncontributory to the general picture.

The mortality of the four therapeutic groups is shown in Table III. In such a small series, mortality figures of themselves mean very little, but analyses have been made of some of the important factors. The area of third degree involvement and also of combined second and third degree is averaged for the fatal cases of the four groups in Table IV.

Table III
Mortality by therapeutic groups

Agent	Total Cases	Mortality, Per Cent	No. Cases with Over 50% Surface Involvement	Revised Mortality, Per Cent
Foille.....	95*	17.8	2	16.1
Tan.....	52*	23.1	3	18.2
Sulfa.....	27	22.2	1	19.2
C. L. O...	11	9.0	0	9.0

* Two burns dressed conjointly with Foille and tannic acid are not included in this tabulation.

Table IV
Average area (in per cent of body surface) of combined 2nd and 3rd degree burns and of 3rd degree alone among fatal cases

Agent	Fatal Cases	Per Cent Combined 2nd and 3rd Degree	Per Cent 3rd Degree
Foille.....	17	26.3	11.6
Tan.....	12	31.7	4.8
Sulfa.....	6	30.3	13.3
C. L. O.....	1	7.0	0.0

Various factors unfavorable to survival occurring in the different therapeutic

Table V
Incidence of factors unfavorable to survival

Agent	Total Cases	Age Under 2 or Over 60	Coincidental Debilitating Disease	Marked Obesity	Degree of Insufficiency of Plasma or Blood	
					Moderate	Marked
Foille.....	95	18	9	1	4	3
Tan.....	52	10	0	4	3	4
Sulfa.....	27	7	5	0	0	1
C. L. O...	11	4	0	0	0	0

groups are set forth in Table v. In Table vi the burns are classified according to the extent of the combined second and third degree involvement. The mortality associated with these varying-sized areas is also shown.

Third degree burns of 10 per cent or more of the body surface are extremely grave. In the present series the following third degree burns of this magnitude survived: *Foille:* 16, 14, 11 and 10 per cent. The average healing time was 120 days.

TABLE VI

PARTITION OF THE THERAPEUTIC GROUPS AS TO EXTENT OF INVOLVEMENT* AND RELATED MORTALITY

Agent	Total Cases	Under 10% Body Surface Involved		10%–15% Body Surface Involved		16%–20% Body Surface Involved		21%–25% Body Surface Involved		Over 25% Body Surface Involved	
		No. Cases	Mortality Per Cent	No. Cases	Mortality Per Cent	No. Cases	Mortality Per Cent	No. Cases	Mortality Per Cent	No. Cases	Mortality Per Cent
Foille	95	57	1.8	18	27.8	5	40.0	5	40.0	10	70.0
Tan	52	34	2.9	8	25.0	3	66.6	0	....	7	100.0
Sulfa	27	18	0.0	2	50.0	1	100.0	2	50.0	4	75.0
C. L. O.	11	9	11.1	1	0.0	0	.....	0	....	0	

* This includes 2nd and 3rd degree burn and is exclusive of 1st degree burn.

A different approach to the problem of mortality is the consideration of the largest surviving burns of each group. There were no survivals in our series with combined second and third degree involvement in excess of 31 per cent of the body surface. The largest surviving second and third degree burns of each series with their healing times are as follows:

Type of Treatment	Combined Second and Third Degree, Per Cent	Third Degree, Per Cent	Healing Time in Days
Foille	22	7	155
Foille	22	16	80
Foille	24	10	146
Foille	27	14	186*
Foille	30	0.5	56
Foille	31	5	98
Tannic Acid	21	2	54
Sulfadiazine	24	10	135
Sulfadiazine	26	5	110

* Patient left hospital with a small granulating pocket in the left axilla, kept open by a severe contracture.

Tannic acid: 12 per cent. Healing was complete in 150 days. *Sulfadiazine*: 11 and 10 per cent. The average healing time was 146 days.

From these mortality and survival analyses Foille, tannic acid and sulfadiazine seem about equally effective in the saving of life. The burns treated with cod liver oil are too few and too small to enter into this evaluation. Our mortality figure for the patients treated with sulfadiazine (22 per cent) corresponds closely to the 20 per cent mortality of Adams and Crawford[16] in their series of fifty cases.

Foille has been criticized on the grounds of the possible toxicity of its phenol content (1.96 per cent). Our clinical impression, as well as the mortality and survival statistics, do not substantiate this criticism. Even one of our fatal cases speaks well for Foille:

D. M., a thirteen-year old girl with nearly 60 per cent of body surface involvement (20 per cent second degree and 40 per cent third degree) lived for thirty-three days. This is the longest survival that we have ever observed

in a burn of this size and severity. Autopsy revealed a large fat-infiltrated liver compatible with chronic sepsis. The kidneys were remarkable only for terminal "cloudy swelling," and failed to show the nephritis that marks chronic phenol poisoning. The other organs were not remarkable.

PROGRESS AND HEALING

Nearly all these cases were personally followed by the writer to final healing. If a patient left the ward too early in his course, so as to leave an undue balance of his healing to Out-Patient Clinic or home, he was discarded from the comparative series.

precipitate which is readily wiped away with moist, sterile pledgets or washed off in a tub. With the entire lesion thus exposed for inspection, the trimming away of the softened necrotic corium, where it begins to loosen, is facilitated and pus pockets are easily found and unroofed. This "open" type of treatment is especially applicable to burns of the face, hands, genitalia and joint creases where a constricting indurated eschar is particularly objectionable. Also, burns eighteen hours and older, already potentially infected, should not, we believe, be sealed up with an eschar. In this connection it was observed by Koch[22] that in the

TABLE VII

AVERAGE NUMBER OF DAYS UNTIL 3RD DEGREE BURNS SURGICALLY CLEAN AND UNTIL ALL BURNS HEALED

Agent	3rd Degree Burns Surgically Clean		All 2nd Degree Burns Healed		Heavy 2nd Degree Burns Healed		3rd Degree Burns Healed	
	Cases	Days	Cases	Days	Cases	Days	Cases	Days
Foille	33	24.0	38	24.3	30	26.9	44	64.0
Tan	12	26.3	26	21.7	17	24.8	15	85.0
Sulfa	16	25.1	7	19.0	5	24.4	17	74.7
C. L. O	3	19.3	6	22.2	5	20.8	4	65.0

Table VII presents two endpoints: (1) days elapsed until the third degree lesions become "surgically clean" or, in other words, free of slough and fit for pin-point grafting, and (2) days elapsed until final healing of the burns grouped according to their depth.

The Sloughing Stage of Third Degree Burns. It had been our clinical impression that burns treated with Foille rid themselves of slough sooner than those dressed with other agents. The figures (Table VII) do not support this to a significant degree. However, the sloughing period in burns treated with Foille can be more efficiently and easily managed and with less pain to the patient than is the case with leatherized burns. At the daily toilette of the burn there is no adherent dressing or tough eschar to be removed; only the soft curdy

French and Belgian hospitals during the present war, burns over twelve hours old and those received at the front were treated by the Lohr cod liver oil method. It would seem from what has been said that the Foille routine would serve even better than vitamin oils, since in addition to being a bland ointment, Foille is more antiseptic, especially the modified preparation containing 1.5 per cent sulfathiazole.

Final Healing. It will be seen in Table VII that there was a significant reduction of healing time in the third degree burns treated with Foille over those treated by tanning or by the sulfanilamide spray. This superiority is especially important since the healing of third degree lesions of any size is the most difficult problem of burn treatment. Whether the cod liver oil therapy was as efficient as it appeared can

only be judged by a larger series involving more serious burns. The average area of third degree involvement of patients followed to healing is indicated below:

	Per Cent of Body Surface
Foille	1.6
Tannic acid	1.0
Sulfadiazine	1.8
Cod liver oil	1.1

Healing of second degree burns came slightly earlier among the leatherized burns than among those treated with Foille. However, these superficial lesions heal satisfactorily regardless of the local application.

An analysis of the incidence of factors unfavorable to healing occurring within the different groups is shown in Table VIII. The

TABLE VIII
FACTORS UNFAVORABLE TO HEALING

Agent	Total Cases	Unfavorable Anatomical Location or Poor Co-operation of Patient		Burns 18 Hours Old or Older. Potentially Infected	
		Cases	Per Cent	Cases	Per Cent
Foille	100	10	10.0	18	18.0
Tan	54	8	14.8	6	11.1
Sulfa	30	2	6.7	3	10.0
C. L. O	11	0	....	0	

first heading includes burns handicapped in healing either by their unfavorable location or because the patient persistently traumatized or soiled them. Burns untreated for eighteen hours or longer were most often placed on Foille therapy, since this agent seemed naturally adapted as a dressing for infected or potentially infected lesions.

Bilaterally-Treated Burns. Seven patients with bilaterally comparable burns were treated simultaneously with two agents, one on either side. Two of these, M. H. and S. F. died (Table I) and will not be considered here. The other five are summarized in Table IX. The first four cases were pin-point grafted. The sulfadiazine-dressed side of S. L., (Fig. 3) in spite of its slower healing, had received one more grafting than the Foille side. It is to be noted than V. M. developed a 10 per cent flexion contracture of the knee on the side that had been tanned. Foille, on the whole, appeared superior to the control agent in these few cases.

Temperature Reaction. In Figure 4 the average highest daily temperature and pulse for the first twenty days have been charted for all second and third degree burns involving 5 per cent or more of the body surface. The burns treated with Foille seemed to show significantly higher temperature reaction than did the other groups during the first eight to ten days. This is difficult to explain. It is apparently not on an infectious basis since the temperature curve made a rapid climb during the second and third days and was on the decline after the fourth day. The Foille pulse curve coincided more nearly with those of the other groups. Since the mortality and survival figures for patients treated with Foille compare favorably with those of the other groups, this early febrile reaction apparently does not bespeak serious morbidity or prognosis.

Delirium. Instances of delirium or mental disturbance were found only among those patients treated with Foille or sulfadiazine. There were thirteen cases in the Foille group (13.7 per cent) and four cases among the sulfadiazine patients (14.8 per cent). One patient treated with both Foille and sulfadiazine was irrational. Two of the Foille cases were delirious within the first three days, the remainder anywhere from the fifth to thirty-sixth days. Three of the sulfadiazine cases fell within the first two days, the fourth on the sixth day. The temperature in nine cases from both groups ranged from 103° to 106°F.; however, in six it did not exceed 101°F. The blood level of one of the patients treated with sulfadiazine was 30 to 31 mg. per cent of the drug during her delirium, but she recovered. The blood level in the others was below 10 mg. per

cent. The mortality of these delirious patients of both groups was 66.6 per cent.

Bacteriology. Routine cultures were taken one or more times (exclusive of the initial one) in 108 cases and the important organisms are set forth in Table x. Staphylococcus aureus was found alone slightly more often than in combination with Streptococcus hemolyticus. The latter was recovered alone in but one instance. Although these routine cultures, streaked out on blood agar, were neither entirely accurate nor representative of all the organisms present, nevertheless it is doubtless significant that 70 per cent of burns treated with sulfadiazine were free of streptococci, whereas a much lower percentage were streptococcus-free in the burns treated with Foille and tannic acid. In short, sulfadiazine seemed to be somewhat more bactericidal than any of the other agents, at least for Streptococcus hemolyticus.

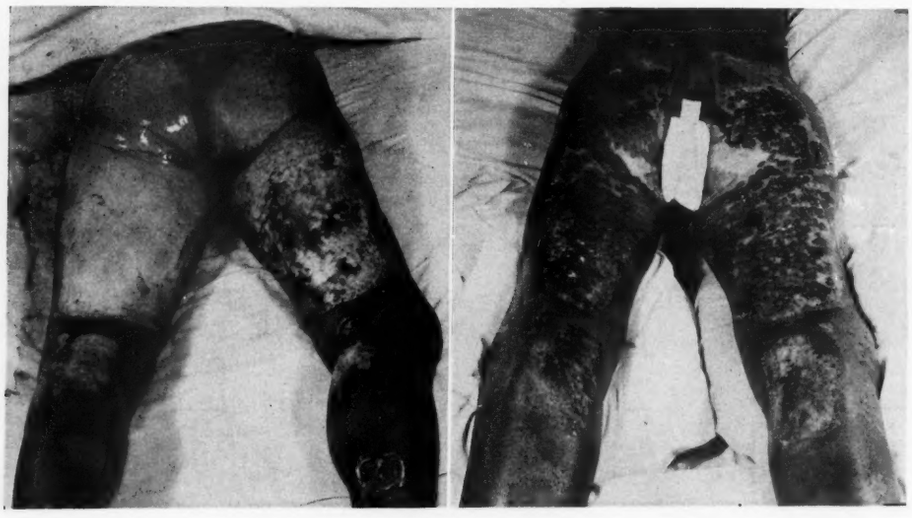
Pain Control. Evaluation of the different agents in respect to their relief of pain during the early days of the burn (Table xi) revealed no outstanding difference between them, although the tannic acid was somewhat superior in this respect and cod liver oil somewhat inferior. The initial application of tannic acid and silver nitrate, however, may be extremely painful. Patients frequently complained to a varying extent of burning for five or ten minutes after each sulfadiazine spray during the first forty-eight hours. It is our clinical impression that the sloughing stage was

TABLE IX

BURNS BILATERALLY TREATED WITH TWO AGENTS

Agent	Name	Age	Degree of Burn and Per Cent Surface Involved	Area Involved	Days Till Ready to Graft	Days Till Healed	Healing and Remarks
Foille.....	V. M.	13	6% 2nd 2% 3rd	Back of left thigh and leg	?	190	The Foille side was well in the lead when pustules developed on both sides; flexion contracture 10° on tan side
Tan.....	"	"	" " " "	Back of right thigh and leg	?	179	
Foille.....	H. C.	5	3% 2nd	Right foot and ankle	..	18	At discharge a few small crusts on both sides; still some tenderness and induration on tanned side
Tan.....	"	"	1½% 2nd	Left foot and ankle	..	18	
Foille.....	S. L.	58	8% 3rd	Left thigh and buttock	30	101	At final healing, slightly more tightness in gluteal region on Foille side, but the involvement had been slightly more extensive
Sulfa.....	"	"	6% 3rd	Right thigh and buttock	35	111	
Foille.....	M. M.	31	3% 2nd 1% 3rd	Right thigh and groin	13	43	Good healing on both sides, but more active on Foille side
Sulfa.....	"	"	7% 2nd 1% 3rd	Left thigh, abdomen and breast	17	68	
Foille.....	S. C.	2	2½% 2nd	Right buttock	..	17	The two burns were identical; progress and final healing were identical
Sulfa.....	"	"	2½% 2nd	Left buttock	..	17	

definitely less painful for patients dressed with Foille than for those otherwise treated. The soft, curdy Foille coating was readily removed at the periodic wound toilette and there were no adhering outer dressings to take off.



A B

FIG. 3. Patient S. H. with nearly identical second and third degree burns of both buttocks and thighs, her left side treated with Foille, her right side with sulfadiazine. A, appearance about fifth hospital day; B, photograph one-hundred first day; Foille side healed; several unhealed patches (outlined in ink) remain on sulfadiazine side.

TABLE X
INCIDENCE OF STAPHYLOCOCCUS AUREUS AND STREPTOCOCCUS HEMOLYTICUS IN BURNS

Agent	Staphylococcus Only		Staphylococcus and Streptococcus		Streptococcus Only	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Foille	25	44.6	30	53.6	1	1.8
Tan	12	48.0	13	52.0		
Sulfa	17	70.8	6	25.1		
C. L. O.	2	66.6	1	33.1		

End Results. This is difficult of evaluation and follow-up. It has been our clinical impression that deeper burns, especially those of the face, hands and flexures, heal somewhat more kindly and with less tendency to contracture when treated with Foille than with any other agent. Figures 5, 6, 7 and 8 illustrate the results obtained with the Foille treatment of severe burns of the hands and face. In general, however, the type of healing and the presence or absence of contractures in the third degree burns of this series depended more upon when and how successfully the skin graft had been carried out than upon the local application chosen. It is inexcusable to omit or put off skin grafting because some favorite vulnerary reputedly "stimulates healing."

TABLE XI
PAIN CONTROL

Agent	Total Cases	Control of Pain, Per Cent		
		Good	Fair	Poor
Foille	81	61.7	29.7	8.6
Tan	37	70.3	24.3	5.4
Sulfa	23	65.2	26.1	8.7
C. L. O.	9	55.5	33.3	11.1

CONCLUSIONS

It should be recalled that one purpose of this study was to find a treatment adapted to conditions far from ideal, such as prevail

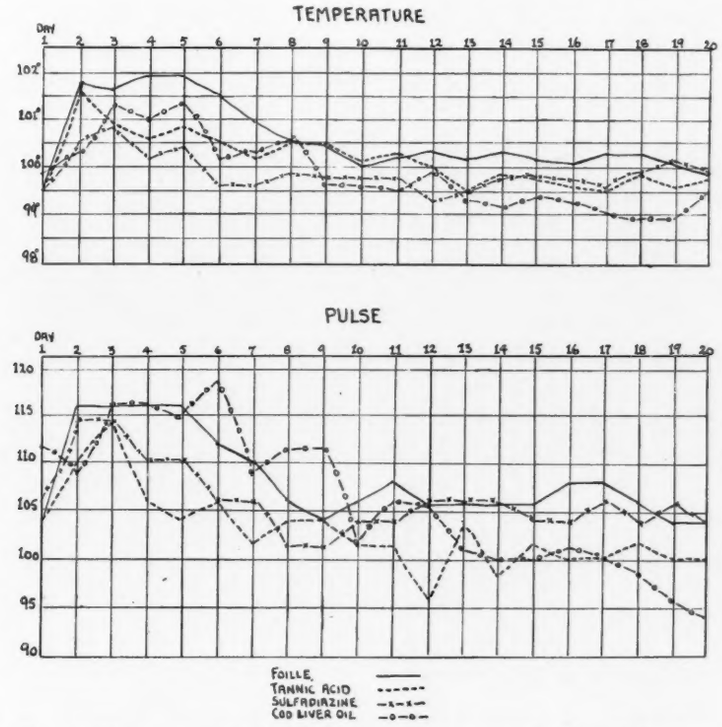
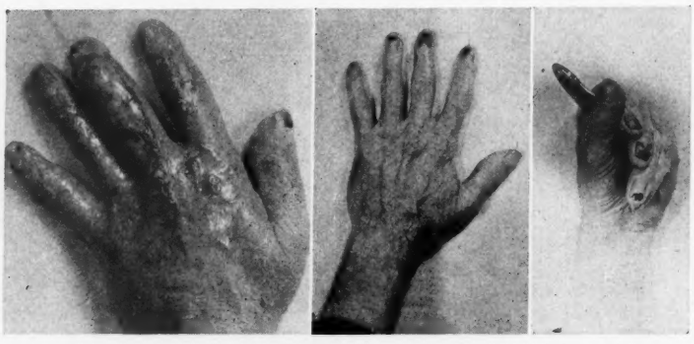


Fig. 4. The average highest daily temperature and pulse of the four therapeutic groups for the first twenty hospital days.

A B

Fig. 5. Patient C. F. with deep second and third degree fire burns of face, hands, arms, chest and thighs treated with Foille. A, just after removal of initial Foille compression dressings, the fourteenth hospital day. Note the third degree burns of the forehead and hands. B, just before final healing; the hands have been pinch-grafted.

in understaffed charity institutions or military hospitals in war time. No mere local application is a substitute for special nurses, close meticulous surgical care and elaborate equipment.



A B C

Fig. 6. Patient W. R. with deep tar burn of extensor aspect of left hand. The extensor tendon of middle finger was exposed and partially sloughed. Treated with Foille. A, appearance when healing was well underway, about the thirtieth day; B and C, shortly after final healing, which occurred the ninety-fifth day.

The therapeutic problems presented by second and third degree burns are vastly different because of the total destruction of corium and skin-regenerating powers in the latter. Second degree lesions aseptically treated will heal kindly regardless of the agent used. We have found nothing superior to combined tannic acid and silver nitrate for simplicity and effectiveness. The sulfadiazine eschar, though more antiseptic, requires too long to form and is definitely inferior to that of tannic acid, when the burned surface is subject to maceration, distortion or pressure.

I agree with Crile[23] that the sloughing stage of the deeper burns is one of inevitable, even if low-grade, sepsis. It presents the problem of early-as-possible removal of the gray necrotic corium, of unroofing underlying pus pockets and of timely skin graft. In our experience this stage is much more simply and efficiently dealt with if there is no tough eschar in addition to the human leather or dermis to be removed. So far at least Foille has approached nearer the ideal than the other agents during this phase, although we have not yet given the Lohr treatment sufficient trial. Applied alone and without other dressings, it forms a soft, protective, mildly antiseptic coating that thoroughly permeates all crevices and pockets. This aids in softening the leathery corium and is easily sponged or soaked

A B

Fig. 7. Patient T. H. with very deep second degree fire burns of both hands and forearms treated with Foille. A, appearance about the seventh hospital day. B, appearance shortly after final healing on the twenty-third day.

away at the daily toilette. No anesthetic has ever been required for the periodic débridements in Foille patients.

4. Foille is superior to the other agents as a dressing for deeper burns, in the following respects: (1) Simplicity of application; (2) it significantly reduces the healing time of third degree burns; (3) it acts as a detergent for grease and oil, and (4) it forms a soft, mildly antiseptic, easily changed coating, ideally suited to infected burns, to burns of the hands, face and genitalia, and to the sloughing stage of third degree burns.

A B

Fig 8. A, patient D. B. with deep second and third degree gasoline explosion burns of face, chest, arms and hands, just after removal of initial Foille compression dressing on fourteenth day. B, same patient just after healing on the seventy-third day. Note the newly healed "postage stamp" skin grafts on left hand and arm.

Needless to say, Foille is not beyond improvement. Promising modifications of the original régime are the initial compression type of dressing and the incorporation of 1.5 per cent sulfathiazole in place of the oxyquinoline. Whether this preparation will prove superior to a simpler sulfonamide ointment, only further investigation will show. So far it has proved a rational and valuable agent.

SUMMARY

1. A comparative study has been made in 199 burns of four topical applications: Foille, tannic acid, sulfadiazine and cod liver oil.

2. These agents are of about the same value in the saving of life.

3. Superficial burns, correctly treated, heal kindly whatever the local application. Here the tannic acid and silver nitrate treatment has the advantage of simplicity.

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For perforating wounds of the abdomen the use of cyclopropane with an intratracheal tube is indicated if a gas is used as an anesthetic agent.

SYNDROME OF ACUTE APPENDICITIS*

THE FREQUENCY OF OTHER CONDITIONS RESPONSIBLE FOR SYMPTOMS

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THE syndrome ascribed to acute appendicitis is not specific for the disease, and indeed, conditions which can give rise to this symptom-complex constitute an impressive list.[1] Fortunately, the diagnosis can be made in the majority of cases.[2]

The low morbidity and mortality subsequent to the removal of the unruptured appendix is apparent in most statistics, and has properly swayed the surgeon toward early operation.[3] There is still, however, a tendency on the part of some practitioners to delay operation until a "definite" diagnosis can be made. Appendicitis is a protean disease with manifestations which are often baffling, and this temporization caused by uncertainty as to diagnosis on the part of the physician, and occasionally the failure of the patient to secure early consultation, often results in complications such as perforation with peritonitis or abscess, considerably augmenting mortality and morbidity figures. Recently, the use of sulfanilamide in these conditions has been of great value.

It has been shown that the risk of early operation in cases of suspected appendicitis is small. Because of this many patients are legitimately explored only to find that the syndrome suggestive of appendicitis was due to some other pathologic condition, or occasionally nothing is found grossly to account for the symptoms which presented.

One hundred cases from the Second Surgical Service of the Mount Sinai Hospital, New York City, were investigated, in which the clinical picture was so strongly suggestive of appendicitis that operation was performed within twelve, and in most instances within six to eight hours after admission, but in which exploration failed to reveal any evidence of acute appendiceal inflammation. Cases of this type were taken consecutively as they occurred over a period of five years and nine months during which time some 1100 operations for appendicitis were performed on this surgical service. The survey was conducted in an attempt to discover from the clinical record and the operative findings the presence and frequency of pathological conditions which could be held accountable for symptoms. While these cases so selected constitute errors in diagnosis, in most instances they are not errors in judgment.

Of the one hundred cases examined, 83 per cent were less than thirty years of age, 60 per cent being under twenty. That the great majority (69 per cent) were females is to be emphasized. There was a history of previous attacks of abdominal pain in 38 per cent. On admission, sixty-five had a history of generalized or midline abdominal pain with a subsequent shift to the right lower quadrant in forty-four. Eighty-eight cases began with or subsequently developed right lower quadrant pain. Nausea occurred fifty-four times, actual vomiting, forty-nine. Rectal tenderness was elicited in sixty-five instances. Forty-three of seventy-two patients in whom a white blood count was performed showed a leucocytosis (over 10,000 per cu. mm.).

It is to be stressed that while urgent operation was considered indicated in all cases, the possibility of other conditions being present was often entertained, as the list of admission diagnoses shows. (Table 1.)

* From the Second Surgical Service of Mount Sinai Hospital, New York City.

TABLE I
DIAGNOSIS ON ADMISSION

Acute appendicitis	77 times.
Acute appendicitis (?), with simultaneous diagnoses of	
Pelvic condition (?)	15 times.
Urinary tract disorders (?)	2 times.
Other diagnoses (?)	6 times.

Of sixty-four cases followed from three months to three years after operation, three patients, all of whom had shown no pathological condition at exploration, had subsequent recurrent attacks of right lower quadrant pain, two were proved to have gallstones, and one continued with clinical evidence of ileocecal tuberculosis, recognized at operation. Two patients required re-operation for acute intestinal obstruction secondary to adhesions. Follow-ups in other patients were negative.

From the clinical data and the findings at laparotomy, it was possible to establish the presence of conditions accountable for symptoms in 55 per cent of cases. (Table II.)

The pathological conditions found may be separated into three large groups: (1) cases of acute mesenteric lymphadenitis, (2) acute ovarian conditions, and (3) a miscellaneous group.

Seventeen cases of acute mesenteric adenitis were encountered. Of these, three were less than ten years of age and fourteen were between ten and twenty-two. An almost equal sex incidence was found (male nine, female eight). Six, or one-third of the patients, had had previous attacks of abdominal pain. Only four presented the classical shift of pain to the right lower quadrant. Vomiting occurred seven times, diarrhea, six. Of interest is the high incidence of rectal tenderness, occurring in thirteen of seventeen cases, being generalized in seven and right-sided in six. Eleven of seventeen cases in whom blood counts were performed showed a leucocytosis of more than 10,000.

At operation free fluid was found in the peritoneal cavity in five patients. All seventeen showed definite enlargement of the mesenteric nodes draining the ileocecal region. The appendix, although grossly normal, was removed in every case; and while all were reported by the pathologist as showing "chronic appendicitis," the additional anatomic finding in six of these cases of lymphoid hyperplasia of the appendix, is to be noted. There were no instances of sequelae in cases followed up to three years.

TABLE II
FIFTY-FIVE CASES WITH PATHOLOGICAL CONDITIONS ACCOUNTABLE FOR SYMPTOMS

Condition	No. of Cases	Remarks
Acute mesenteric adenitis	17	9 male, 8 female
Acute ovarian conditions	16	13 right, 3 left
Rupture of Graafian follicle without hemorrhage	3	
Rupture of Graafian follicle with intraperitoneal bleeding	6	
Ruptured corpus luteum cyst with intraperitoneal bleeding	4	
Hemorrhage into corpus luteum cyst	3	
Pelvic inflammatory (tubal) disease	3	2 acute, 1 chronic
Acute right pyelonephritis	2	
Cholelithiasis	2	
Acute gastroenteritis	5	
Miscellaneous pathological conditions	10	
Acute regional ileitis	2	
Ileocecal tuberculosis	1	
Pericecal granuloma	1	
Acute purulent Meckel's diverticulitis	1	
Carcinoid of appendix with mucocele	1	
Infarcted appendix epiploica of cecum	1	
Intestinal obstruction due to adhesion with infarcted loop of small bowel	1	
Acute right epididymo-orchitis	1	
Acute catarrhal jaundice (jaundice developed on the fourth postoperative day)	1	

Sixteen patients with acute ovarian conditions were operated urgently with symptoms suggesting acute appendicitis. In thirteen, rupture of an ovarian follicle, follicle cyst, or corpus luteum cyst had occurred, usually with bloody or clear fluid present in the peritoneal cavity at

the time of operation (twelve times). In three cases there was acute hemorrhage into a right corpus luteum cyst without rupture into the abdominal cavity.

All patients but one were unmarried. Two-thirds of the group were between eleven and twenty years, the rest being under thirty. Seven had a history of previous attacks of abdominal pain. Only two patients manifested a shift from midline or generalized pain to pain in the right lower quadrant. Two cases had a history of a reverse shift of pain, starting in the right lower quadrant and becoming generalized, said to be suggestive of ovarian conditions. Vomiting occurred in five patients. Rectal tenderness was elicited in nine. White blood counts were performed in twelve patients, and in seven, the white cells numbered more than 10,000 per cu. mm. There were no sequelae in cases followed.

With regard to the third or miscellaneous group, Table II is self-explanatory. Certain cases (e.g., perforating carcinoma of the cecum), in which the appendix is usually not removed, would escape the method of case-finding employed.

COMMENT AND CONCLUSIONS

1. These one hundred patients presented a symptom-complex, centering for the most part about pain and tenderness in the right lower quadrant with a variable, concomitant incidence of nausea, vomiting, fever, and leucocytosis of varying degrees. In each case urgent surgery was deemed advisable and all were explored within twelve hours after admission to the hospital. In no case did exploration disclose acute appendiceal inflammation.

2. Clinical and pathologic evidence, sufficient to account for symptoms, was found in 55 per cent of the cases.

3. Acute mesenteric lymphadenitis, affecting male and female in comparable incidence, constituted a major portion of this group.

4. Acute pelvic conditions, for the most part ovarian, were present in another large number of cases. The preponderance of females in this series was thus partly explained.

5. The large group of miscellaneous pathological conditions needs no additional comment. The low incidence of each of these conditions makes their diagnosis difficult, and many, if recognized, would nevertheless have required operative interference.

6. In 45 per cent of cases no definite acute condition was discovered.

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INTESTINAL ANASTOMOSIS*

DESCRIPTION OF A NEW TECHNIC

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WITH the discovery of the process of intestinal repair by Lembert,[20] and the introduction of asepsis by Lister, intestinal resection began to be accepted as a definite surgical procedure. Reports of successful resections of the colon began to appear toward the end of the nineteenth century. In 1882, Thomas Bryant[3] reported a successful resection of the colon. He was followed by Barton,[2] in 1888; Bloch,[5] in 1892; Paul,[33] in 1895, and Mikulicz,[27] in 1903.

Independently of each other, both Paul and Mikulicz attracted the attention of the surgical profession to the principle of exteriorization. There were slight differences in the technic of exteriorization as practiced by Mikulicz and by Paul. Paul sutured together the ascending and decending bowel loops attached to the tumor, fixed them into the incision, removed the growth and tied a glass tube into the lumen of each sectioned loop. The spur thus formed was crushed and the colostomy later closed extraperitoneally by a plastic procedure. Mikulicz followed a similar technic but did not suture together the bowel loops fixed in the abdominal incision. It is to the credit of both Mikulicz and Paul that they advocated and practiced removal of an adequate portion of the mesentery with the growth at the time of the operation. Unfortunately, sufficient importance was not immediately attached to this feature of the exteriorization principle. Mikulicz[27] was able to report, in 1903, on sixteen resections of the colon using the principle of exteriorization. The mortality was 12.5 per cent. In comparison, he reported on twenty-one cases of resection with primary suture performed in his clinic with a mortality of 42.9 per cent. This mortality was the average mortality for any primary suture of the colon at that time. It is not surprising, therefore, that the principle of exteriorization was so readily acceptable. However, as resections began to be more frequently practiced by exteriorization, the average mortality was found to be much higher than that originally reported by Mikulicz; and yet, never as high as with direct anastomos is.

MORTALITIES WITH EXTERIORIZATION

	Year	Per Cent
Nordmann[30]	1926	28
Cheever[6]	1913	18
MacFee[24]	1937	28
Allen and Welch[1]	1939	21
Finsterer[9]	1939	17
Grinnel[14]	1939	27
Mayo and Simpson[25]	1939	20
Wilkie[46,47]	1939	19
Paterson and Webb[32]	1940	27
Gibbon, Jr. and Hodge[13]	1941	29
Lahey[19]	1941	13
Average mortality		22.9

It was soon realized that if further progress was to be made in lowering the morbidity and mortality and raising the operability, other factors would require consideration. The enormous amount of experimental and clinical data which began to accumulate indicated the necessity of distinguishing between obstruction in the upper and lower intestinal tract on the one hand, and whether or not there existed an interference with the circulation on the other. The results of bowel obstruction on the physiological economy also became

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apparent. Finally, it has become possible to formulate certain principles, the practice of which has contributed immeasurably toward making bowel resection a safer procedure. Briefly considered, these factors are as follows:

Fig. 1. Basting stitch is being placed below crushing clamp holding end of resected bowel. This stitch is both hemostatic and prevents soiling.

Fig. 2. The basting stitch has been completed. A half loop is in the process of formation.

Relief of Obstruction. Whether decompression of the bowel is obtained by intubation with a duodenal tube or a Miller-Abbott technic or some form of direct bowel drainage, the same purpose will have been fulfilled. The effects resulting from a compromised circulation, and the absorption of toxic products through a weakening mucosa will cease. This is a most important preoperative measure for both large and small intestinal obstruction, provided that there has been no vascular mischief.

Restoration of Biochemical Imbalance to a More Normal Status. Dehydration and nutrition are readily overcome by saline and glucose infusions. Hypoproteinemia and anemia are combatted by the administration of plasma and whole blood. Vitamin deficiency is restored by the appropriate administration of the necessary vitamins. Laboratory tests can quite accurately determine when this restoration has taken place.

Local Cleansing of the Bowel by Lavage and the Preoperative Use of Chemotherapy. In every resection of the colon, these preoperative measures are very important. A definite control of infection in the bowel can thus be exercised. Devine,[8] in his procedure of obstructive resection, has been an ardent advocate of such measures and has suggested using cod liver oil to be instilled into the defunctioned colon. The sulfa drugs have already been shown to play an important part in the preoperative phase. Garlock and Seley[11] were the first to report in 1939, the beneficial effect of sulfanilamide in resections of the colon, controlling Streptococcus hemolyticus organisms. Nine resections of the colon were reported with one death which was not due to peritonitis. Lockwood and Ravdin[22] reported similar

favorable experiences. Then in December, 1940, Firor,[10] using a new sulfa drug—sulfanilguanidine—reported his experience in difficult resections of the colon with no fatalities and no peritonitis. In some of these cases gross soiling and contamination had occurred.

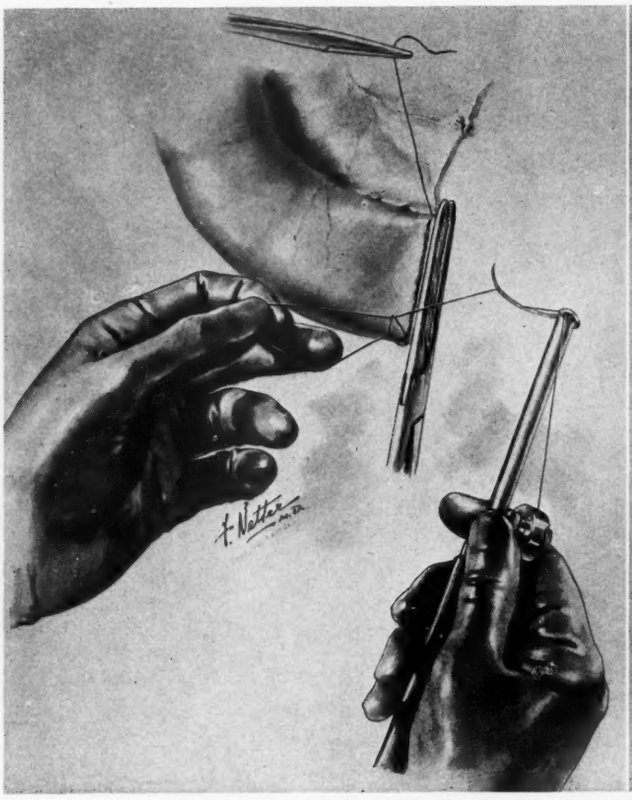

FIG. 3. Detail of half loop fixing the stitches temporarily.

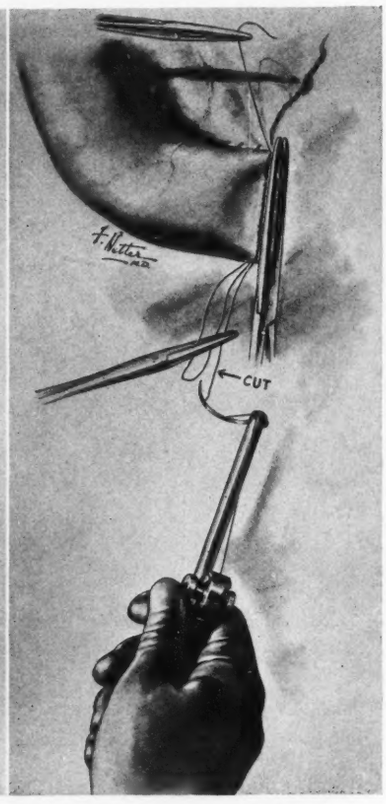

FIG. 4. The strands of the half lock stitch are held as traction sutures. The loop and single strand are so arranged that the entire basting stitch can readily be removed by pulling on the single strand alone.

Accuracy and Care in Operative Technic. It is important that no resection be performed unless the bowel has been adequately mobilized. In this way, tension at the suture line will be avoided. Wilkie[46] even suggests dividing the longitudinal muscular bands so that the strain on the suture line will be equally distributed over its entire circumference. With the use of the closed method of anastomosis, a meticulous technic will reduce infection to a minimum. Both theoretically and practically, it is an ideal procedure for bowel resection.

In the consideration of every bowel resection there are certain intrinsic problems. Not the least of these is the local blood supply. In resections of the small intestine, because of the rich collateral circulation and generally good blood supply, both axial and lateral anastomoses can be practiced without fear of a vascular compromise, if the proper technic has been used. In the colon, however, it has been shown that the circulation is practically terminal in type, and that as the distal portions of the colon are approached, the vascularity diminishes.

Meillere,[26] Lockhart-Mummery,[21] Stewart and Rankin,[43] and others have pointed out the special features of the blood supply of the colon. Based on these observations, it has been suggested that in resections of the colon, the antimesenteric edge be made shorter than the mesenteric because the blood vessels run at right angles to the long axis of the bowel. The possibility of

necrosis in the suture line may thus be avoided. Infection, early and late, resulting in peritonitis, retroperitonea infection, and local abscess formation has been the greatest problem. If the circulation is adequate at the time of the operation, it may become inadequate through faulty suturing as occurs sometimes in the technic of exteriorization, or it may follow too much suturing in the performance of a direct anastomosis. Both Wilkie and Devine have advised only a single tier of stitches in direct anastomosis of the colon.

Knowing how readily anaerobic organisms thrive on devitalized tissue, there is also the possibility of a spreading gangrene from this source causing a leak in the suture line. The introduction of the newer forms of chemotherapy may overcome some of these problems. Other factors to be considered causing a leakage through the suture line are the early liquifaction of catgut and vitamin deficiency in delaying the process of repair. It makes little difference whether a lateral, axial or terminal lateral type of anastomosis is used. Surgical experience has demonstrated that actually there is little difference in mortality between axial or lateral anastomosis. For instance, Miller,[28] in 1923, found a higher mortality with lateral than with end-to-end anastomosis in resections of the colon for carcinoma. Raiford,[36] in 1935, found that the operative mortality with lateral anastomosis was almost three times greater than with the end-to-end technic. There are, however, two serious objections to the lateral anastomosis: the one is that the blind pouches may elongate resulting in fecal stasis; and the other is that leakage may occur from the pouches themselves. On the other hand, the method interferes very little with the intrinsic blood supply of the colon and gives adequate peritoneal surfacing.

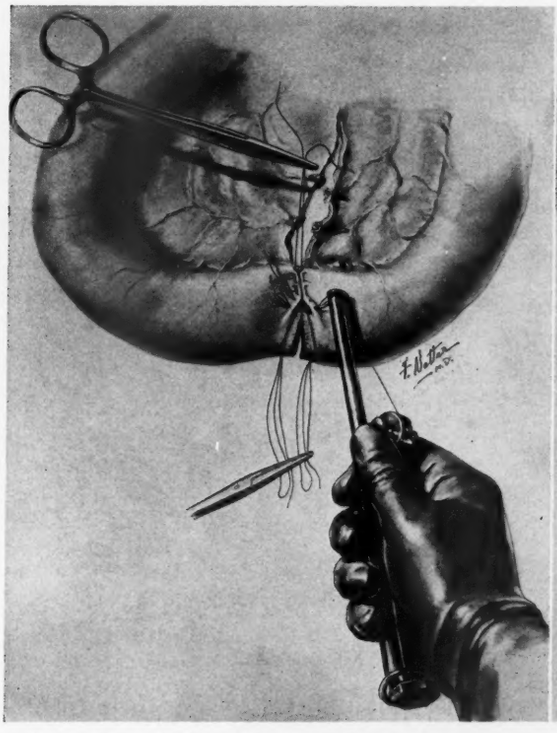

Fig. 5. The placing of horizontal mattress sutures approximates cut ends of bowels over the basting stitches on each end of bowel.

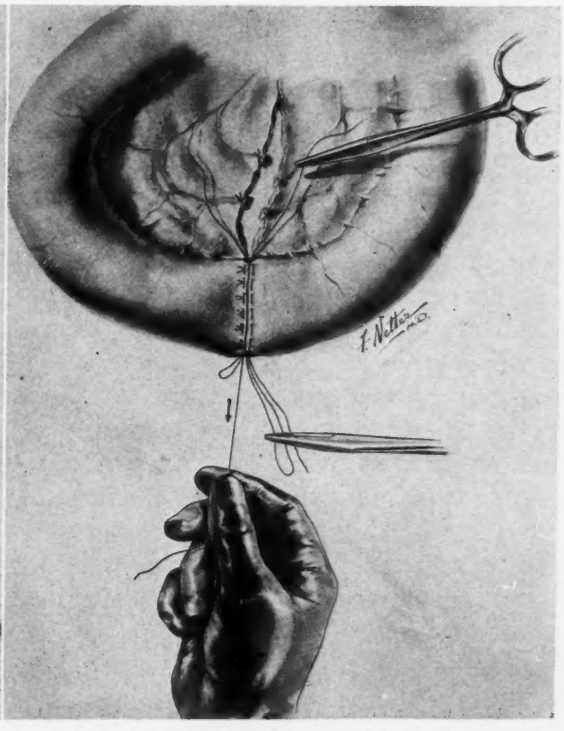

Fig. 6. The single strand is now being pulled out. Notice the corresponding loop becoming smaller. With the removal of both of these basting stitches, the temporarily closed ends of the bowel will again be open. The technic of the aseptic anastomosis has now been completed.

There are two basic methods of bowel resection: (1) exteriorization, and (2) direct anastomosis, open or closed. These methods have been used in resections both in the small intestine and the colon. Due to rapid dehydration and the loss of vital tissue fluids, direct anastomosis, with very few exceptions, is the method of choice for resections of the small intestine. In resection of the colon, both of the above methods are practiced.

The principle of exteriorization consists of mobilizing the bowel sufficiently to permit its safe fixation in the abdominal incision after the removal of the affected tumor. An adequate area of mesentery is resected at the same time to remove lymphatic structures when the operation is performed for malignancy. The antimesenteric edges of the two limbs are sutured together and fixed in the wound and the tumor is then removed. A variety of clamps are used to keep the stomas closed and help in their wound fixation. Rankin[39] has described such a device. Sometimes a small catheter is implanted into the proximal segment beneath the clamp to control distention and permit it to be left on longer. The peritoneum is carefully sutured about the limbs of the colon to effect complete closure. After twenty-four hours, the spur is crushed with an enterotome converting the double barrel into a single barrel colostomy. Sometimes this colostomy will close spontaneously, but most often a plastic closure becomes necessary later.

The principle of exteriorization has also been advocated in right colon resections to restore continuity between the ileum and the transverse colon.[18] This method, however, has been used mostly in resection of the sigmoid. There are surgeons who will use it in cases of dilated and distended bowel in which the possibility of postoperative infection from leakage through the suture line may occur. It has been claimed that it is the preferred procedure in elderly patients because the procedure is graded. The prolonged convalescence which increases the risk of cardiovascular renal complications and which from an economic viewpoint, may be a hardship to the patient, is hardly an argument for exteriorization as a graded operation. It is interesting to note that after many years of experience with this method that its use is becoming less general. There are several reasons for this changed attitude: (1) The technical limitations prevent sufficient radical extirpation of the bowel and mesocolon for malignancy except in a limited group. (2) It is often impossible to mobilize the sigmoid sufficiently in fat and elderly patients to permit fixation of the colon in the wound.

The procedure, therefore, cannot be considered very flexible in its application. With the placement of the ends of the colon in the incision without proper mobilization, the resulting tension may cause a leakage through an unfortunately placed fixation suture, or subsequent retraction of the stomas toward the peritoneal cavity, may cause an opening in the peritoneal cavity resulting in peritonitis. Infection often occurs in the wound delaying healing. Many of these patients, after recovery, will have weak abdominal wounds which may later result in hernia formation.

Cheever,[6] in reporting a series of resections of the colon, states that the average hospitalization with direct anastomosis was forty days. When using the principle of exteriorization, the hospitalization period was fifty-six days. Mayo and Simpson,[25] in reporting their experiences, state that for resection and primary anastomosis, the period of hospitalization was twenty days as compared to fifty-nine days with exteriorization. It is also interesting to note in Cheever's report that 50 per cent of the patients treated by direct anastomosis were healed on discharge and 27 per cent had a fecal fistula. With the exteriorization technic, only 30.7 per cent were healed on discharge and 53.8 per cent had a fecal fistula. Rankin,[37] in 1930, in reviewing a large series of cases using the exterioriza-

tion principle, reported a recurrence in the wound of 12 per cent. This is another serious disadvantage of the operation.

The principle of exteriorization is surgically sound. Its usefulness will be determined by its own special limitations. Because of the objections cited above and the advances made in our being able to recognize and combat the serious changes resulting from intestinal obstruction, attention has again been drawn to the method of direct anastomosis. Based upon our newer knowledge of physiology and biochemical imbalance, it has been possible to prepare patients adequately pre-operatively so as to permit a primary resection and direct anastomosis.

DIRECT ANASTOMOSIS—OPEN METHOD

	Year	Per Cent
MacFee[24]	1937	18.8
Gibbon, Jr. and Hodge[13]	1941	38
Allen and Welch[1]	1939	23
Stone and McLanahan[44]	1939	26
Mayo and Simpson[25]	1939	11
Cheever[6]	1913	15.3
Average mortality		22

ASEPTIC ANASTOMOSIS

	Year	Per Cent
MacFee	1937	16
Wilkie[46]	1934	12
Allen and Welch	1939	11
Stone and McLanahan	1939	11
Gibbon, Jr. and Hodge	1941	13
Gibbon[12]	1932	20
Schoemaker[41]	1921	8
Average mortality		13

It will be noted from studying the table that the mortality using this principle is about the same as the mortality with the Mikulicz procedure without the many disadvantages of the latter. One must bear in mind that a primary resection and direct anastomosis presupposes today a careful preoperative preparation as outlined above.

There is still considerable prejudice toward the use of direct anastomosis as a routine procedure, particularly with resections of the left colon. The principle has been criticized because of the possibility of introducing infection during performance of the procedure. Furthermore, there was the possibility of delayed leakage through the suture line because of a compromised circulation. These criticisms are particularly leveled at axial anastomoses. Furthermore, it has been feared that an axial anastomosis will not function properly. Joll[15] states that in over 200 cases, he has not had a single failure of a properly functioning axial anastomosis. The objection that with an open anastomosis there is little control over the possibility of infection is a valid one and has been so recognized. Over 200 methods of anastomoses have been described in the literature, truly an indication of what this problem holds for the surgeon in his efforts to control infection. According to Gibbon, Jr. and Hodge,[13] since 1908, forty-six of the 200 methods are of the so called "aseptic type." The term "aseptic anastomosis" is inaccurate. Many of these methods so described in reality consist rather of procedures to control the possibility of infection at operation and reduce it to a minimum. Very few can be strictly classified as aseptic. The term "closed anastomosis" would be more correct. Even though some contamination may occur during the performance of such a procedure, it never becomes the same problem as when suturing is performed through the exposed lumen of the bowel. It must now become evident that the closed method must be given the attention which it heretofore has been denied. The method about to be described is both simple and practical.

TECHNIC

This closed method of anastomosis is based upon three principles: (1) The placement of a certain type of lateral locked stitch which effectively controls bleeding and leakage, whether from the resected

colon or small intestine below the clamps holding the resected ends of the bowel; (2) hardly any devitalized tissue need be included in the anastomosis; (3) the size of the diaphragm is extremely small, because the approximation is made over a suture and not over clamps. This technic of anastomosis has been found applicable for axial, lateral and terminal lateral anastomoses, not alone of the bowel proper but in subtotal gastrectomy in place of the dePetz clamp.

In this technic, a lateral locked stitch is placed with the Singer Surgical Stitching Instrument a few millimeters below the clamp holding the resected bowel. The beginning of this stitch is not tied, but is held in a fixed position by means of a small anchoring hemostat. When this stitch has traversed the full width of the bowel, it is temporarily fixed by an incompleted half lock stitch as shown in the illustrations. From experience gained with the use of this method, the crushed portion of the bowel held in the clamps, was removed before beginning the anastomosis. The illustrations show the original technic in which this crushed tissue was not removed. By removing this devitalized tissue, it is believed that the possibility of infection in the suture line can be reduced still more. In using this particular type of retaining stitch, it has been found that after the anastomosis has been completed, the size of the resulting diaphragm is very small. After the mattress sutures have been placed as shown in the illustrations, the clamp is released from the incompleted half locked stitch. By pulling on the retention stitch in the same direction in which it was placed, it will be found that it can be pulled out with the greatest of ease. Finger manipulation to make certain of the patency of the anastomosis completes the operation. The amount of contamination which has resulted in suturing through the entire bowel thickness apparently has not made the least material difference as far as infection is concerned. There is no important difference when using this technic for colon resections. The appendices epiploica may offer some problem here, but by carefully dissecting them back and not too deeply so as not to injure the underlying terminal artery, the surgeon can easily dispose of this problem. This technic can be used equally well with silk, cotton, nylon or fine chromicized catgut.

The rôle of the Miller-Abbott tube for relieving distention in the small intestine proximal to the suture anastomosis has been found to be extremely helpful in promoting a smooth postoperative course. When direct anastomosis was practiced on the colon, a cecostomy was found to be less efficient and dependable in accomplishing a thorough cleansing of the bowel and in controlling distention above the suture line. The obstructive colostomy as advocated by Devine, has been found to be the method of choice for effectively decompressing and cleansing the colon. Furthermore, the suture line was protected by the obstructive colostomy against exposure to all infectious matter until it had been demonstrated that adequate healing was present.

Advantages. The advantages claimed for this technic of closed anastomosis are the following: (1) This lateral lock stitch is readily placed with the Singer Surgical Stitching Instrument. (2) This retention stitch effectively controls leakage and hemorrhage from the resected ends of the bowel. (3) In certain situations in which accessibility is limited and crushing clamps are placed with difficulty, a double row of retention stitches may be placed and the bowel transected between them, very much in the manner after the placement of the staples by the dePetz instrument. (4) Hardly any crushed tissue need be turned in when making the anastomosis. Thus infection in the suture line can be minimized because no devitalized tissue will exist to encourage bacterial growth. (5) Because of the characteristics of this stitch in being sparing with the amount of tissue it requires for its placement, only a very small diaphragm is formed at the site of

anastomosis. (6) This technic is applicable to various sized structures. (7) The retention stitch is readily removed without incurring tissue trauma. (8) The same instrument, by changing the needle, may be used for making the anastomosis and closing the incision. No other special instruments are required.

SUMMARY

A comparison is made between the principles of exteriorization and direct anastomosis. The respective advantages and disadvantages of the Mikulicz-Paul procedure are given. The importance of preoperative preparation which forms the basis of modern colon surgery are briefly reviewed. Continued clinical experience is beginning to favor direct anastomosis; particularly, as we have begun to understand better the problems of intestinal obstruction and how to combat them effectively. It is suggested that the term "closed anastomosis" be substituted for "aseptic anastomosis." A new technic of closed anastomosis is presented and its advantages outlined.

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The anesthetist should try to overcome the tendency to make multiple thrusts with the needle while injecting but little solution (10 cc.). Less trauma results if the needle is introduced slowly and the solution is injected rapidly.

THE USE OF SULFAGUANIDINE AS AN INTESTINAL ANTISEPTIC*

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FROM the studies of Marshall and his co-workers[11] on the experimental and clinical use of sulfaguanidine these facts have been ascertained: (1) Although the solubility of the drug in water is greater than that of other sulfonamide compounds, the drug is absorbed less completely from the gastrointestinal tract. (2) The oral administration of the compound reduces the coliform bacteria count in the feces of human subjects. (3) The action of sulfaguanidine is more specific for coliform organisms within the gastrointestinal tract than is that of other sulfonamide drugs. Thus, with regard to specificity and low absorbability, sulfaguanidine would appear to be a desirable therapeutic agent against the most common bacteria of the large bowel, the coliform organisms. This opinion has been borne out by Firor,[3] Marshall[10] and Lyon.[9]

TABLE 1

	Gm. of Compound Added to Feces	Gm. Recovered	Per Cent Recovered
Sulfaguanidine....	3	2.91	97.0
Sulfathiazole.....	3	2.83	94.3
Sulfapyridine.....	3	2.81	93.3

Firor has obtained satisfactory results when the drug was administered therapeutically in the preparation and postoperative care of patients submitted to surgery of the colon. Marshall and Lyon[9,10] likewise reported good results in the treatment of acute bacillary dysentery when the drug was administered early in the course of the disease. Although such reports indicate that sulfaguanidine is a useful therapeutic agent, a more extensive experimental and clinical evaluation of the compound is necessary. This communication presents the experience obtained at the Memorial Hospital in the clinical use of sulfaguanidine.

CLINICAL MATERIAL

For this investigation twenty female* and seven male† hospitalized patients were studied. The average age of the entire group was forty-nine years and ranged from thirty-one to seventy-two. All the female patients except one had recently undergone radical mastectomy for carcinoma of the breast, and she had a chronic radiation ulcer of the chest wall. All males had diseases of the rectum or sigmoid colon. In each of the male patients some type of surgery on the colon was done. Six had carcinoma of the colon or rectum and one had chronic diverticulitis. The patient with chronic diverticulitis and two others of the male group had colostomies as a result of previous surgery. The remaining four patients had carcinoma of the colon. They had not undergone any surgical procedure previous to this study.

METHODS

I. Dosage. In order to evaluate the effect of sulfaguanidine 4 Gm. of the compound were administered orally every eight hours to each patient. This dosage is comparable to that used by Firor[3]—50 mg. per kilogram of body weight.

* From the Breast Service of Dr. Frank E. Adair.
† From the Mixed Tumor Service of Dr. George T Pack.

* From the Memorial Hospital, New York City.

II. Laboratory Studies. a. Sulfaguanidine levels in blood and urine were determined by the method of Bratton and Marshall.[1]

The concentration of the free compound in the blood of each patient was determined at least three times weekly. The amount of the acetylated sulfaguanidine in the blood was not measured.

Both acetylated and free forms of the compound were determined in twenty-four-hour collections of urine at least four times weekly in each individual. In addition to the quantitative determination of sulfaguanidine in urine, the urinary sediment was examined microscopically for crystals of the compound.

b. Sulfaguanidine Excretion in Stools. In order to determine the amount of the compound in the feces it was necessary to modify the method of Bratton and Marshall for the determination of sulfaguanidine in urine. This was done in the following manner:

The specimen, collected in a large covered pail, was transferred to a wide-mouthed jar with approximately 1,500 cc. of hot water. Rotary mixing by means of an electric stirrer was carried out for fifteen to thirty minutes until a suspension of uniform consistency was obtained. At the end of this period, the total volume of the fecal suspension was taken and two aliquots of 10 cc. each were measured immediately into graduates for duplicate determinations. Each aliquot was extracted with at least four 50 cc. portions of boiling acetone. The combined acetone extracts were filtered and made to a volume of 250 cc. A 1 cc. aliquot of the yellow filtrate was measured into a test tube containing 0.5 cc. of 8 per cent hydrochloric acid and 8.5 cc. of distilled water. The color was developed as described by Bratton and Marshall.

The following precautions are necessary in order to insure a proper determination: (1) The volume and the aliquots of the fecal suspension must be taken immediately on cessation of stirring; otherwise the suspension will not be uniform. (2) The volume of the fecal suspension must be greater than 1,500 cc. in order that turbidity of the final solution may be avoided.

Calculation:

$$\text{Total Gm. in specimen} = \frac{(s)(cs)}{(u)} \times 0.025 \times \text{volume of fecal suspension.}$$

s represents the reading of the sulfaguanidine standard, u the reading of the unknown, and cs is the concentration of the standard.

c. Hematology. On alternate days determinations of hemoglobin and counts of the erythrocytes, leukocytes and platelets were made.

d. Blood Chemistry. The levels of serum proteins,[22] plasma prothrombin,[23] cholesterol and cholesterol esters,[15] bilirubin and blood urea were determined before, during and after therapy.

e. Bacteriology. A minimum of three stool cultures and colony counts of the coliform bacteria were made of the feces of each patient. These cultures were grown on desoxycholate media. In most patients daily bacteriological studies were made unless for some reason a specimen of feces could not be obtained. An attempt was made in all instances to secure a culture and colony count of coliform organisms in the stool specimen before the drug therapy was started. After administration of the sulfaguanidine was begun no cathartics were given except to those patients who were prepared for surgery of the colon.

A $\frac{1}{10}$ Gm. portion of stool was employed. A $\frac{1}{100}$ dilution of stool previously homogenized with sterile physiological saline was made. Of this dilution 0.1 and 1.0 ml. samples were added to 20 ml. of desoxycholate media and the whole poured into sterile Petri dishes. After forty-eight, seventy-two and ninety-six hours of incubation at 35°C., colony counts on each culture were made.

p-Aminobenzoic acid in concentrations of from 1 to 5 mg. per 100 ml. has been shown to be effective against the bacteriostatic action of sulfapyridine, sulfathiazole

and sulfanilamide.[2,5,8,13,16,19,23] Therefore, 5 mg. of p-aminobenzoic acid were added to 100 ml. of desoxycholate media in order to ascertain whether sulfaguanidine was bacteriocidal or was bacteriostatic for the coliform organisms. Duplicate colony counts were made on the stools using the media containing p-aminobenzoic acid.

RESULTS

The results of this investigation are grouped under the following headings: (1) Studies of the absorption and excretion of the drug; (2) the effect of sulfaguanidine on the coliform bacteria of the bowel; (3) the effect of the compound on the patient; and (4) the use of sulfaguanidine in surgical patients.

Table II

Amount of Drug Given	Recovered in Feces		Recovered in Urine	Total Recovery of Dose Given
	First 3 Days	Second 3 Days		
6 Gm.....	2.50 Gm.	0.91 Gm.	0.76 Gm. 0.67 0.30 0.017	
	3.41 Gm. (56.6%)		1.747 Gm. (29.1%)	85.7%
6 Gm.....	3.38 Gm.	0.54 Gm.	0.5 Gm. 0.4	
	3.92 Gm. (65.3%)		0.9 Gm. (15%)	80.3%

I. Absorption and Excretion: a. Recovery of Sulfaguanidine from the Excreta. In order to demonstrate that sulfaguanidine could be determined satisfactorily, two types of recovery experiments were carried out. First, known amounts of sulfanilamide, sulfathiazole or sulfaguanidine were added to feces from normal individuals. Table I demonstrates that recoveries from 93 to 97 per cent were obtained. Secondly, one dose of 6 Gm. of sulfaguanidine was administered to each of two patients. The urine and feces of each patient were collected and analyzed for the drug over a period of six days. Table II presents the results of the excretion of sulfaguanidine in two patients yielding total recoveries of 80 to 85 per cent.

Had the collection of the excreta been carried out for a longer period, it is believed that a somewhat higher quantitative yield might have been obtained. The somewhat lower recovery of sulfaguanidine after the ingestion of the compound is not due to the presence of the acetylated derivative of the drug, since hydrolysis of several extracts of fecal material from different patients gave no increased color reaction. These results indicate that the method employed is satisfactory for clinical studies.

b. Excretion of Sulfaguanidine in Feces. From Table II it is evident that the amount of sulfaguanidine recovered from the stools varies in each patient. This variation appears to be governed, most likely, by the amount of the compound absorbed from the gastrointestinal tract.

Hubbard et al.[7] have studied two patients with biliary fistula to whom sulfaguanidine was administered. In neither patient was there any evidence to show that appreciable concentrations of free sulfaguanidine occurred in bile. No test for the presence of acetyl sulfaguanidine was carried out.* In order to account for the absence of the acetylated derivative in the feces of these patients two possibilities exist: first, that no appreciable quantity of the acetylated derivative of sulfaguanidine is excreted into the gastrointestinal tract through the bile; secondly, that whatever acetylated sulfaguanidine is excreted with the bile is either hydrolyzed by bacterial action or is preferentially absorbed through the walls of the gastrointestinal tract and excreted in the urine.

c. Excretion of Sulfaguanidine in Urine. The free and acetylated sulfaguanidine excreted by each patient in twenty-four-hour periods was determined by the

* The presence of acetyl sulfanilamide has been detected in bile in small amounts.[6]

method of Bratton and Marshall. In 166 determinations the average total sulfaguanidine excretion in the urine was 1.71 Gm. per day. (Fig. 1.) The average daily urinary excretion of acetylated derivative was 0.25 Gm., or 14.6 per cent of the total.

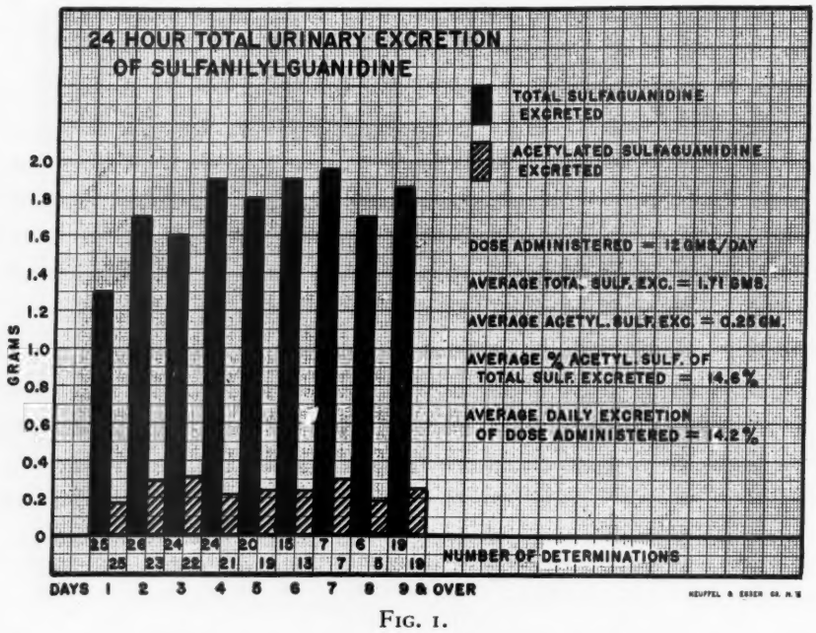
24 HOUR TOTAL URINARY EXCRETION OF SULFANILYLGUANIDINE
TOTAL SULFAGUANIDINE EXCRETED
ACETYLATED SULFAGUANIDINE EXCRETED
DOSE ADMINISTERED = 12 GMS./DAY
AVERAGE TOTA. SULF. EXC. = 1.71 GMS.
AVERAGE ACETYL. SULF. EXC. = 0.25 GM.
AVERAGE % ACETYL. SULF. OF TOTAL SULF. EXCRETED = 14.6%
AVERAGE DAILY EXCRETION OF DOSE ADMINISTERED = 14.2%
GRAMS
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
25 26 24 24 20 15 7 6 19
25 23 22 21 19 13 7 5 19
NUMBER OF DETERMINATIONS
DAYS 1 2 3 4 5 6 7 8 9 & OVER

FIG. 1.

The amount of compound recovered from the twenty-four-hour urine specimens of each individual patient varied considerably. The range found for the patients studied was from 0.2 Gm. to 5.6 Gm. Of the sulfaguanidine administered the average excretion in the urine was 14.2 per cent of the total daily dose. Therefore, despite its solubility the greatest proportion of the compound remains in the bowel in a sufficiently high concentration to act as a local chemotherapeutic agent.

d. The Concentration of Sulfaguanidine in the Blood. The amount of absorption of the 4-Gm. doses of sulfaguanidine administered every eight hours is reflected in the blood levels obtained. The levels here reported are only those of free sulfaguanidine. The blood level concentrations ranged from 2 to 4 mg. per cent, and of ninety determinations, the average was 2.1 mg. per cent. In only two instances was a level of more than 5 mg. per cent (5.6 and 5.8 mg. per cent) found, and in neither of these patients were any signs of toxicity noted. The sulfaguanidine concentration in the blood remained low, probably because that portion of the drug absorbed is excreted rapidly in the urine. Abnormal individual absorption or renal dysfunction may result in an accumulation of the compound in the blood but these variables were not observed in any patients of this series.

II. The Effect of Sulfaguanidine upon the Coliform Organisms. A wide variation in the number of coliform organisms on the culture plates is found normally. In the feces of patients used as controls the coliform organisms ranged from tens of thousands to billions of colonies per ml. of wet sediment of stool. This wide variation was noted also in the control coliform colony count from feces of the patients who subsequently received sulfaguanidine. (Fig. 2.)

The addition of p-aminobenzoic acid to the desoxycholate media did not alter the coliform bacteria counts in 99 per cent of all stool cultures made. When no growth of coliform organisms was found on either type of media, incubation was continued for another four days. After this continued period of incubation further growth appeared on the p-aminobenzoic acid media in only two of 168 cultures. It would ap-

pear, therefore, that when the coliform organisms have not grown upon either type of media after four days' incubation under optimum conditions, no further growth can be expected.

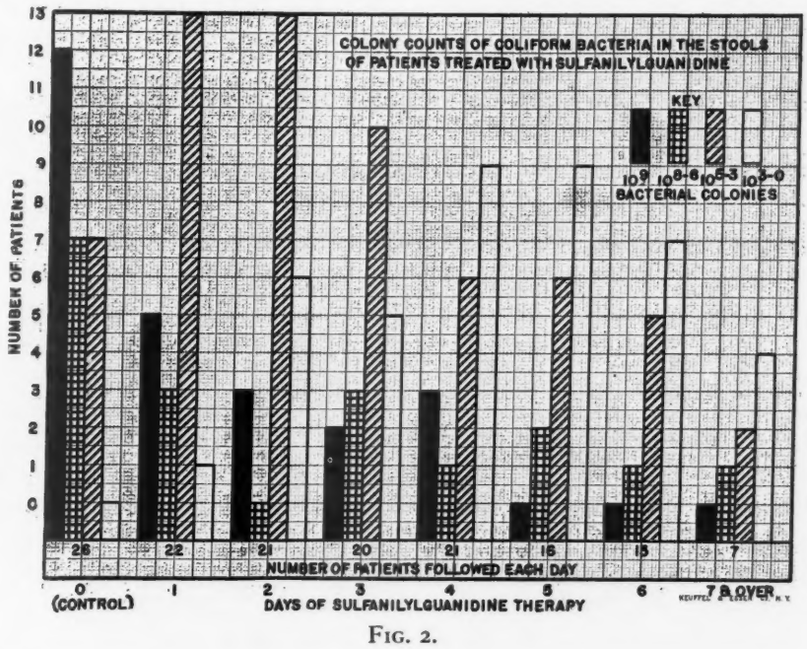
COLONY COUNTS OF COLIFORM BACTERIA IN THE STOOLS OF PATIENTS TREATED WITH SULFANILYLGUANIDINE
KEY
BACTERIAL COLONIES
NUMBER OF PATIENTS
NUMBER OF PATIENTS FOLLOWED EACH DAY
28 22 21 20 21 16 13 7
(CONTROL)
DAYS OF SULFANILYLGUANIDINE THERAPY
7 & OVER

Fig. 2.

When a known sulfonamide inhibitor, p-aminobenzoic acid in concentrations of 1 to 5 mg. per 100 ml., is added to culture media, Janeway[8] has shown that bacteria which are inhibited by the bacteriostatic action of any sulfonamide will grow if any viable organisms are present. From the evidence previously presented, it appears that in those individuals in whom the administration of sulfaguanidine reduced the coliform flora, the action of the compound was bactericidal and not bacteriostatic.

On the whole sulfaguanidine was effective in reducing the number of coliform organisms in the stools. (Fig. 2.) Of twenty-seven patients, eighteen showed a reduction from 10^{9-8} (billions or hundreds of millions) to 10^{3-0} (thousands or no growth) colonies per ml. in the coliform organisms grown from their stools. In the other nine no significant therapeutic effects were obtained.

There was no immediately apparent explanation for the reduction in coliform organisms which was effected in some patients and not in others. The possible explanations are (1) existence of ulcerative lesions within the bowel, (2) the infrequency of administration of sulfaguanidine, and (3) the presence of drug-resistant coliform bacteria in the intestinal flora.

Of the nine patients whose intestinal bacterial flora apparently were unaffected by the administration of sulfaguanidine, four had ulcerative lesions of the sigmoid colon or rectum. The presence of a sulfonamide inhibitor in pus and in other autolysed tissues has been demonstrated.[12] The exudate from an ulcerated bowel lesion may be of such quality, or exist in such quantity, that it will neutralize the bacteriostatic or bactericidal action of sulfaguanidine. It has been shown also that the clinical course of patients with chronic ulcerative colitis is not affected by sulfaguanidine.

After the administration of sulfaguanidine to three patients who had colostomies with intact mucosa above the stoma, satisfactory reduction in coliform bacteria was noted. This result indicates that when the mucosa is intact good therapeutic responses are obtained. Therefore, a marked reduction in coliform organisms can be obtained in the segments of colon above the sigmoid and rectum. This fact may be

important from a prophylactic standpoint. If an ulcerative lesion in the sigmoid is removed surgically, the line of anastomosis thus will not be bathed with intestinal contents which contain excess coliform organisms. Such organisms are inhibited likewise in the postoperative period when sulfaguanidine is administered.

No explanation is at hand for the failure of sulfaguanidine to reduce the coliform bacteria count in the stools in the remaining five of nine patients. It was not determined whether or not the intestinal bacteria of those five were abnormally resistant to the drug.

From the accumulated data* it is evident that no constant reduction in the total number of coliform organisms were obtained. Neither was there any uniformity in the rate of reduction of the bacteria. In several patients it was found that after therapy had been administered for several days the number of coliform organisms was decreasing rapidly. Then, for some unknown reason, the colony count would increase temporarily to about pre-therapy levels, but eventually would decrease again and remain at low levels. In some instances no coliform organisms could be cultured from the last stool specimen examined.

In summary, a noticeable effect of sulfaguanidine upon the coliform organisms usually was apparent from three to four days after therapy was instituted. The colony counts remained low after that time except for the occasional culture in which there appears to be an "escape" from the bactericidal action of the drug. The maximum effect of continued sulfaguanidine therapy is obtained within five to six days. When therapy was discontinued a steady rise in the coliform bacteria count began and reached pre-therapy numbers in two to three days.

It would appear, therefore, that the optimal time for surgery of the colon in patients who receive sulfaguanidine as a prophylactic agent would be from five to seven days after the use of the compound was started. Theoretically, the postoperative sulfaguanidine therapy should be started from twelve to twenty-four hours after surgery.

III. The Effect of Sulfaguanidine on the Patient. a. Effect on the Blood. Complete blood and platelet counts were done on alternate days in the patients studied. Neutropenia, agranulocytosis or hemolysis never were noted. In only one patient was a significant change found in the hemogram after the administration of sulfaguanidine.

In that one patient a reduction of the hemoglobin from 65 to 49 per cent (normal 13.8 G) was associated with a fall in the erythrocytes from 3.5 to 2.9 millions. There was no significant reduction in the leukocytes. This anemia developed after administration of 48 Gm. of the compound given over a period of four days. The blood level of sulfaguanidine was never above 0.5 mg. per cent and no rise in bilirubin was noted. There was no evidence of hepatic dysfunction as determined by an increased ratio of cholesterol to cholesterol esters, or by a fall in the concentrations of serum proteins or plasma prothrombin. Subsequently, a study of the bone marrow revealed it to be moderately hypoplastic. Unfortunately, a bone marrow examination had not been made before sulfaguanidine therapy.

Since the amount of the compound absorbed by this patient was only 1.7 Gm. and represented only 3.4 per cent of the total dose administered, it was probable that the patient was sensitive to the drug. The anemia persisted for four weeks despite the parenteral administration of 45 units of concentrated liver extract per week and ingestion of 45 gr. of ferrous sulfate per day.

b. Effect on the Liver. In order to detect the possibility of hepatic damage after use of sulfaguanidine the following studies were made:

In twenty-two of the patients serum protein values were determined both before and after sulfaguanidine therapy. Five

* Due to lack of space a large table presenting all the data outlined in the text of this article has not been included.

patients had pre-therapy levels below the normal value of 6.5 Gm. per 100 ml. Significant decreases in the serum protein values below the initial values were not found in any patient.

In eighteen patients the ratio of free to total cholesterol in the serum was likewise determined before and after therapy. A normal ratio of from 25 to 33 per cent was noted in every patient.

In sixteen patients no retention of bilirubin was observed.

In twenty six patients the plasma prothrombin was determined. A decrease of prothrombin values of 20 per cent was considered to be significant. Five of the twenty-six patients developed significantly low levels during the course of sulfaguanidine therapy.

It was important, therefore, to determine whether the development of hypoprothrombinemia was due to hepatic damage[17,18,21] or to some other cause. It has been accepted that vitamin K is synthesized from dietary factors by the activity of bacteria in the intestine,[4,14] and it was possible that the administration of sulfaguanidine destroyed those organisms in the intestine which are responsible for the synthesis of vitamin K. To ascertain the facts concerning this question two of the five patients with hypoprothrombinemia were given 2 mg. of synthetic vitamin K_1 (2-methyl-1, 4-naphthoquinone) parenterally. The administration of this compound was followed in both by a rapid return of the plasma prothrombin values to the pre-therapy levels. The three other patients were not given vitamin K, but when the sulfaguanidine was discontinued a rise in the plasma prothrombin levels followed within four days. This experiment would indicate that the hypoprothrombinemia which followed sulfaguanidine administration was not due to a deranged fabrication of prothrombin by the liver, but to a decreased synthesis of the vitamin K by the intestinal flora. This conclusion is supported by the finding that in every patient who showed a decrease in plasma prothrombin a significant reduction in the coliform bacteria count of the stools was found.

The values of serum proteins, the ratio of free to total cholesterol, and the values of bilirubin and plasma prothrombin, determined in a significant number of patients, indicated that no significant alterations in liver physiology could be attributed to the use of sulfaguanidine.

c. Renal Function. Despite the fact that a relatively small percentage (14.2 per cent) of the total amount of sulfaguanidine administered was excreted in the urine, signs of renal irritation were encountered in three patients. Each of these three showed microscopic hematuria which disappeared in three days after the fluid intake was increased. In the urine of one patient casts of sulfaguanidine crystals were found, and this cylindruria was associated with tenderness over the left kidney.

At some time during therapy every patient had sulfaguanidine crystals in the urine, but the number of crystals present varied considerably.

The blood urea concentration was determined in twenty of the twenty-seven patients. No patient developed concentrations of blood urea above those initially found.

d Other Toxic Manifestations. Of the other signs or symptoms which might be attributed to the use of sulfaguanidine, only nausea, vomiting and vertigo were encountered. Nausea and vomiting were observed in two patients, but were not severe enough to make it necessary to discontinue therapy. Two patients complained of vertigo, but no other findings were present to suggest irritation of the central or peripheral nervous systems. Cyanosis, skin eruptions, or the development of fever or jaundice never were seen.

IV. Use of Sulfaguanidine in Surgical Patients. In seven patients surgery of the colon was done. Briefly, the case histories of these patients are as follows:

Case 1. This patient had a large ulcerated carcinoma of the rectum. After six days of sulfaguanidine therapy the effect upon the

coliform organisms was equivocal. There was evidence of renal irritation. Many red blood cells were found in the urine together with a large number of crystals of sulfaguanidine. The tumor was inoperable. A colostomy was made. The patient made an uneventful convalescence.

Case II. This patient had an extensive ulcerated carcinoma of the rectum. With three days of therapy no effect on the coliform organisms was noted. The tumor could not be resected. A colostomy was made. There were no postoperative complications.

Case III. This patient had a one-stage abdominoperineal resection for a large ulcerated carcinoma of the rectum. No effect on the coliform organisms was noted after four days of sulfaguanidine therapy. Renal irritation was indicated by the presence of many red blood cells and crystals of sulfaguanidine in the urine. The contents of the resected loop of bowel was cultured and a colony count for coliform organisms showed 100,000 colonies. The convalescence was uneventful.

Case IV. This patient had a resection of the sigmoid for carcinoma with establishment of bowel continuity by a primary aseptic type of anastomosis. After three days of preoperative sulfaguanidine therapy there followed a reduction of the bacterial content of the stool from a count of billions to one where no coliform organisms were found by culture in the stool specimen taken just previous to surgery. Sulfaguanidine was not administered postoperatively. The patient had an uneventful convalescence and was discharged on the sixteenth postoperative day. The bowel content of the resected loop was cultured and contained four million colonies of coliform bacteria per ml. of wet sediment. This patient illustrates the difficulty which is encountered in the evaluation of the effect of sulfaguanidine. It is quite possible that this patient would have done well without sulfaguanidine therapy.

Case V. This was a seventy-two-year-old male who had two previously unsuccessful attempts at closure of a colostomy which followed a Mikulicz type of resection for carcinoma of the transverse colon. A large ventral hernia with a marked protrusion of the bowel had developed around the midline colostomy.

After six days of sulfaguanidine therapy the stool culture contained only 1,000 colonies of coliform organisms. The peritoneal cavity was opened. A side-to-side *open* anastomosis of the loops of colon leading to the colostomy was made, and the large colostomy stoma was closed. The entire colon was replaced in the peritoneal cavity. Seven Gm. of sulfanilamide were placed along the lines of anastomosis. Sulfaguanidine was started twenty-eight hours postoperatively. The postoperative temperature was 101°C. on the first postoperative day, and thereafter never over 100°C. No signs of peritoneal irritation developed and the wound healed per primam. In this instance the drug probably did contribute to the smooth convalescence.

Case VI. This patient was given sulfaguanidine for sixteen days before closure of a colostomy. This colostomy had been constructed as a result of a Mikulicz resection of the sigmoid for chronic diverticulitis and bowel obstruction. A marked reduction in coliform bacteria had been effected by sulfaguanidine therapy. The operative wound healed per primam without any signs of inflammatory reaction about the wound. On the eleventh postoperative day a small fistula developed but readily closed without further operative interference. This patient had not received the drug during the postoperative period.

Case VII. After seven days of drug therapy the stool count for this patient was reduced from millions of colonies to 3,000 colonies on the day preceding surgery. The colostomy was closed and sulfaguanidine was continued postoperatively. The first stool specimen, passed five days after surgery, showed the absence of coliform organisms. The prothrombin value decreased to 50 per cent. Two mg. of 2-methyl-1,4-naphthoquinone were given parenterally and the prothrombin increased to 81 per cent.* The wound healed per primam without any trace of inflammatory reaction. The temperature was never over 100°C. at any time during convalescence.

The effect sulfaguanidine had upon the clinical course of these patients is difficult to evaluate. Any or all of the patients may have done well regardless of the prophylactic use of the drug.

DISCUSSION

The problem of the adoption or rejection of a new member of the sulfonamide

* This patient is not considered in the group of patients discussed previously, as surgery may have been a contributing factor in lowering the prothrombin value.

group must be approached by determining whether or not the compound really is useful therapeutically in a group of conditions for which it was proposed. It is also necessary to discover the fate of the compound, its actual mode of action, and whether or not its therapeutic administration is attended by the production of any toxic effects on the patient.

From the studies presented of absorption and excretion of the compound, it is evident that there is a marked variation in the amount of compound absorbed in each individual patient. However, unlike other sulfonamide compounds in general use, sulfaguanidine is relatively poorly absorbed from the gastrointestinal tract. Thus it remains in the bowel in a sufficiently high concentration to act as a local chemotherapeutic agent. That portion of the compound absorbed is rapidly eliminated in the urine and high blood concentrations are not usually found.

Sulfaguanidine therapy did produce a marked effect upon the coliform intestinal flora in a significant number of patients. Alteration of the intestinal flora in some patients appears to retard the synthesis of vitamin K in the bowel and hypoprothrombinemia results. Reduction of coliform bacteria by sulfaguanidine in the adult results in a condition analogous to that found in hemorrhagic disease of the newborn. The prompt establishment of a bacterial flora in the newborn causes a rise in the prothrombin, probably as a result of the production of vitamin K.[14] Likewise the withdrawal of sulfaguanidine is followed by an increased number of coliform organisms and a rapid rise of the plasma prothrombin to normal values.

Although no patient developed a hemorrhagic crisis, a tendency to such a complication might well have been present. It is, therefore, important that the plasma prothrombin level be checked routinely before patients are subjected to bowel surgery when sulfaguanidine has been administered preoperatively.

In this study sulfaguanidine did not cause any abnormalities in the hepatic functions measured, namely, the maintenance of a normal ratio between the free and esterified cholesterol, excretion of bilirubin, and the synthesis of serum protein and plasma prothrombin.

Sulfaguanidine may be toxic to the hematopoietic system of some patients. This finding was observed in but one instance in this study.

Although signs of renal irritation were observed in three patients, it appears fortuitous that no serious renal complications were encountered, as crystalluria was present in every patient. Oliguria, retention of nitrogenous products or signs of renal colic were never observed.

When the volume of urine excreted is low, crystalluria might present a serious hazard. The low solubility of the acetylated sulfaguanidine might lead to precipitation of crystalline deposits along the urinary tract. The maintenance of a sufficiently high fluid intake, therefore, is imperative in order to prevent massive crystalline concretions.

Other toxic manifestations in this study were relatively unimportant. The rapid elimination of the absorbed portion of the compound through the urinary tract may explain the infrequency of general toxic manifestations.

The experience obtained here of the practical application of sulfaguanidine to bowel surgery is limited. The compound appears to be of some value in selected cases. This conclusion is in agreement with the experience of Firor. Prophylactic use of sulfaguanidine thus far has its greatest merit when administered to patients who are prepared for surgery of the colon. The drug is much more effective when there are no ulcerative lesions of the bowel. Sulfaguanidine may be expected to be of use in uretero-intestinal anastomosis, closure of colostomy stomas, and in restoration of bowel continuity in the two-stage types of colonic resections when the bowel may have to be replaced in the peritoneal cavity.

In most patients a reduction in the number of coliform bacteria in the stools can be expected. In those patients whose coliform flora are not diminished markedly, the toxicity of sulfaguanidine is not sufficient to preclude its trial.

Further work on a large number of patients is needed to establish that rôle the prophylactic use of sulfaguanidine might play in the reduction of morbidity and mortality in elective surgery of the colon. The fact is to be emphasized that a rigid control study of the effect of sulfaguanidine on the bacterial flora of the bowel must be made in every instance.

SUMMARY AND CONCLUSIONS

1. A method for determination of sulfonamide compounds in the feces is presented. A mean average of 14.2 per cent of the total administered compound is eliminated in the urine. Usually the blood level concentrations remain low, probably because the drug is rapidly excreted in the urine.

2. The administration of sulfaguanidine markedly reduced the coliform organisms in the bowel in eighteen of twenty-seven patients.

3. When ulcerative lesions of the bowel are present, a significant reduction in the coliform organisms is not obtained. This fact would limit the beneficial results which could be expected from the use of the drug.

4. The use of sulfaguanidine resulted in an alteration of the blood picture in only one of twenty-seven patients. Nevertheless, it is advisable to check the blood counts of those who receive the compound in order to detect the occasional patient whose hematopoietic system is sensitive to sulfaguanidine.

5. The administration of this compound caused no other significant toxic reactions in twenty-six of twenty-seven patients.

6. Sulfaguanidine by its action of depressing the coliform bacteria interferes with the synthesis or absorption of vitamin K in some patients.

7. Crystalluria with subsequent formation of concretions might be considered a hazard but this complication can be overcome by giving adequate fluids.

8. Sulfaguanidine is not the ideal chemotherapeutic agent for intestinal antisepsis. A sulfonamide which can destroy all the intestinal bacteria and yet have the slow absorption and low toxicity of sulfaguanidine is to be desired.

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Cervical block, deep or superficial, should be completed about twenty minutes before the incision is to be made so that the nerve trunks can become sufficiently affected. Sometimes relaxation of the cervical muscles is so marked after the cervical nerves have been blocked that the patient cannot move his head without moving his shoulders.

FIVE YEARS OF GALLBLADDER SURGERY IN A GENERAL HOSPITAL*

A REVIEW OF 337 CONSECUTIVE GALLBLADDER OPERATIONS

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THE 337 cases included in this review were approached with the primary purpose of studying the pathological findings as a basis for understanding the thirty-five deaths which occurred. The end results obtained in 302 patients, the "living" series, were evaluated.

Queens General Hospital is the only all-municipal hospital serving a population of about 1,300,000 in the Borough of Queens in New York City. The bed capacity is 700 and the average hospital stay is nine days. Annually, the autopsy percentage has been consistently over 58 per cent, with about 500 house autopsies being performed each year.

The types of cases studied were divided arbitrarily into those without jaundice, both chronic and acute, and patients having definite jaundice at the time of operation. The "chronic" cases had the typical history and physical findings of chronic gallbladder disease, confirmed pathologically. Classed as "acute" were cases having a typically acute clinical course with a pathological diagnosis of acute disease. Cases having the clinical features of chronic gallbladder disease with the findings of acute pathological conditions at operation were also classified as "acute." Comprising the third major group were patients in whom obstructive jaundice was present at the time of operation, with either an acute or chronic gallbladder condition being found. All cases in which carcinoma was implicated were eliminated from consideration.

I. BASIS OF THE STUDY

The conclusions reached from this study were based on three principal sources of information: the pathological changes in the gallbladder, the causes of death, and the follow-up study.

The pathological changes in 306 gallbladder specimens were studied by the Department of Pathology with gross and microscopic analysis. The surgeon's description of his findings was the only report available for thirty-one cases in which neither cholecystectomy nor postmortem examination had been performed. *The causes of death* were studied at autopsy in twenty-four of the thirty-five patients who comprised the "death" series (68 per cent). Clinically, eight of the remaining eleven had "reasonably certain" factors in death, such as frank signs of spreading peritonitis or of cardiac failure. In three cases, factors in deaths were considered "probable." At a series of twelve *follow-up clinics* held specifically as a part of this study, 180 patients were interviewed and examined. Twenty-two questionnaire reports were received through the hospital's Volunteer Motor Corps which visited the homes of ninety patients who had failed to respond to repeated calls by mail. In forty-seven additional cases, notes were made available by previous clinic visits. By these methods a follow-up percentage of 75 per cent was obtained. The unreported 25 per cent, however, was proportionately distributed among the three main types of cases. Of

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the 229 "chronic" cases, 168 responded (73 per cent); of the forty-four "acute" cases, thirty-seven responded (84 per cent); and of the twenty-nine "jaundiced cases," twenty-four responded (82 per cent). Reliable comparisons of the results in each group could thus be made.

II. THE "DEATH" SERIES

A. Mortality Rates. Table I, covering the mortality rates in the various groups,

TABLE I
MORTALITY RATES

Type Case	Sex	No. of Cases	Survived	Died	Mortality Rate, Per Cent	Combined M and F, Per Cent
Chronic without jaundice, 241 cases.	F	206	200	6	2.9	4.9
	M	35	29	6	17.0	
Acute without jaundice, 56 cases.	F	39	31	8	20.5	
	M	17	13	4	23.5	21.4
Jaundiced acute and chronic, 40 cases.	F	35	27	8	22.8	
	M	5	2	3	60.0	27.5
Total	..	337	302	35	10.0	

indicates a low mortality rate in the largest group, chronic cholecystitis. The rate of 2.9 per cent among the females and the combined rate of 4.9 per cent compare favorably with the results obtained elsewhere. Carter et al.[1] reported a 3.6 per cent mortality rate for their chronic cholecystitis group. While in our series, "acute" cases had a mortality rate of 21 per cent, cases with jaundice at the time of operation proved more fatal (27 per cent). The table also shows the higher mortality rates among males. Cases in which deaths occurred were, in general, of an emergency nature. (Table II.)

B. Factors in the Mortalities. Study of the clinical and autopsy records showed the presence of several factors common to two or more deaths.

1. *The age and sex factors* can be considered together. (Fig. 1.) The death rate for elderly patients was higher than for those in the younger age groups. The males were generally older than the female patients.

TABLE II
GENERAL EMERGENCY NATURE OF THE CASES IN WHICH DEATH OCCURRED

	Death Series 35 Cases, Per Cent	Living Series 302 Cases, Per Cent
1. Cholecystograms		
a. Done	32	69
b. Not done	68	31
2. Jaundice	31	9.6
a. With fever	54	17
3. Incidence of acute pathological conditions	45	21
a. With perforation	17.1	3
4. Incidence of cardiacs	41	5.6
5. Incidence of patients over 50	51	35

2. *The cardiac factor* in mortality appeared frequently. Definite heart disease was present in fifteen of thirty-five cases (41 per cent). Operation precipitated frank cardiac failure with fatal result in two patients, both apparently well compensated before operation. Especially among the cardiac patients under fifty years of age, heart failure was an important contributing factor to death. In all, nine surgical deaths could be attributed, at least in part, to the cardiac factor. In sharp contrast was the low incidence of heart disease among the patients who survived operation. Only seventeen of 302 patients (5 per cent), had a diagnosis of heart involvement made preoperatively and frank failure occurred only once.

3. *The factor of acute gallbladder disease* played a significant rôle. Acute inflammatory changes were present in sixteen cases among the deaths. Figure 2 shows its age distribution and emphasizes its more frequent occurrence among the "death" group and in the elderly male. An acute pathological condition was the main factor in death in seven of thirty-five patients. Subdiaphragmatic abscess, subhepatic ab-

scess, right lower lobe lung abscess with empyema and extensive peritonitis were some of the findings in three cases.

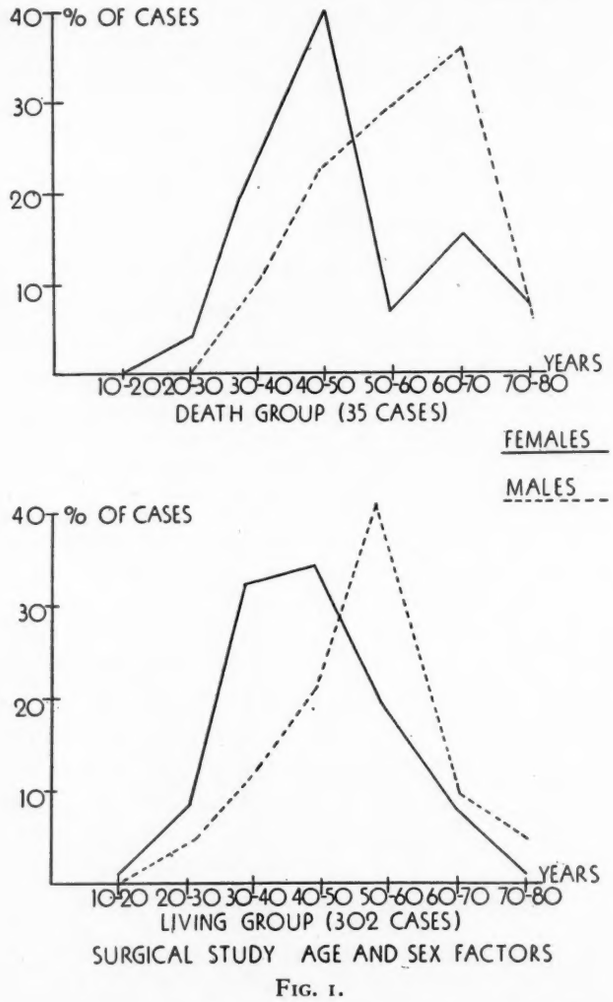

Fig. 1.

4. Closely linked to acute pathological lesions was the factor of *perforation of the gallbladder*. While this occurred relatively infrequently in the series of 337 cases (2.3 per cent) it was much more common (12 per cent) when acute cases were considered and still more frequent (27.2 per cent) when empyemas of the gallbladder alone were considered. Only two cases of perforated gallbladder were listed among the living. Thus of eight perforations, six resulted fatally (80 per cent). These findings emphasize the importance of perforation of the gallbladder as a factor in operative mortality.

5. The factor of *chronic gallbladder disease* was significant mainly because it gave rise to the impaction of stones in the biliary ducts, to the fibrotic occlusion of the ducts and to the development of marked liver damage with biliary cirrhosis. Impacted ampullary stone was associated with two cases of fatal acute pancreatitis. Three instances of chronic pancreatitis were noted but this lesion seemed to be of little importance in the final analysis of these three deaths. Marked hepatitis was noted likewise in three cases. Obstructive jaundice resulted from fibrotic occlusion of the common duct twice and from impacted common duct stone in seven instances. No obstructing calculus could be found in two cases. The rôle jaundice played as a factor in fatality will be subjected to further analysis.

6. *The accidental factor in the mortalities* was of considerable importance. There were ten deaths that could be traced to it. necrosis of the right hepatic lobe, occurred once, as did a duodenal tear with resulting peritonitis and a sudden death under

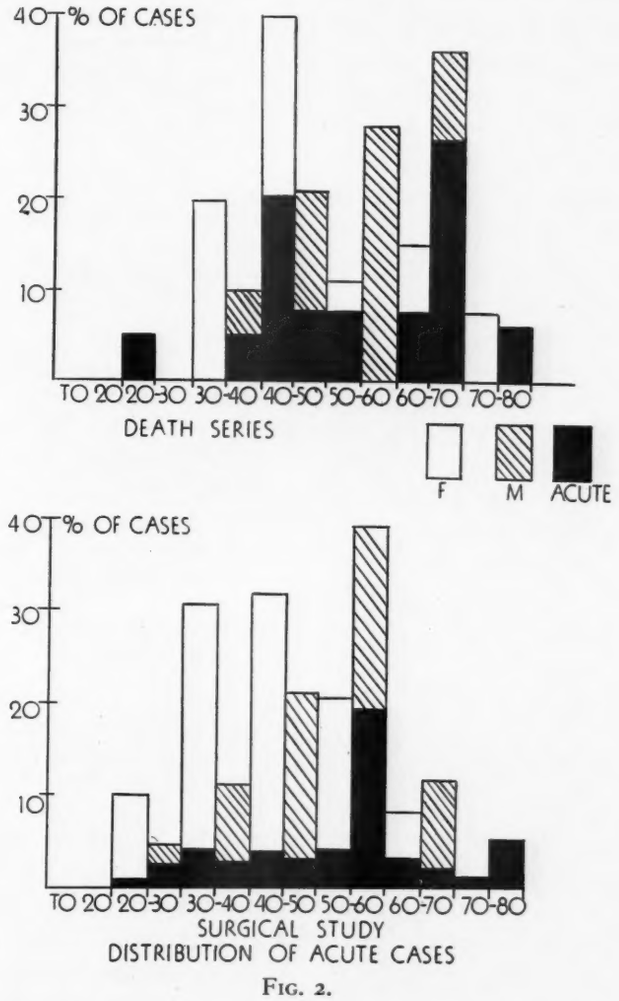

Fig. 2.

Each of these patients had postmortem examination performed. Postoperative hemorrhage caused five deaths. The site of the bleeding vessel could not be found even at autopsy in two of these. Venous varices of the common duct were identified as the source of bleeding in two others and laceration of the portal vein in the remaining one. Common duct injury was noted in two cases. One was a case of injury at a previous operation, with death resulting from a long series of complications all due to fibrotic occlusion of the duct at the site of original injury. The other was a case of accidental mass ligation of the common duct. Ligation of the right hepatic artery, with massive spinal anesthesia before operation was begun.

7. The factor of *concomitant serious disease* was important in several deaths, though not directly related to gallbladder disease. Extensive bronchopneumonia accounted for three deaths. Each of the following was of great importance in one case: bronchogenic carcinoma with widespread metastases, concomitant ruptured appendix with generalized peritonitis, concomitant carcinoma of sigmoid colon producing intestinal obstruction, a ruptured colonic diverticulum with peritonitis and a fulminating erysipelas involving a postoperative wound.

8. *Bacteriological* reports were not available in every case. Bacillus coli was the most common offender in patients who died following extension of acute inflammatory processes. The occurrence of a pure culture of Friedlander's bacillus in one fatal case was considered of special interest. Other organisms encountered in this study included Bacillus typhosus, hemolytic streptococcus, nonhemolytic streptococcus, Streptococcus viridans, Bacillus pyocyamus, hemolytic staphylococcus aureus, and Bacillus alkaligenes.

9. The *diabetic* factor in the mortalities was not apparently of great significance. Five of the thirty-five patients who died were diabetics (11 per cent), as compared to eight of 302 patients (2.6 per cent) in the living series. Scrutiny of the factors of deaths among these diabetic patients, however, disclosed that postoperative pneumonia, carcinoma of the lung, cerebral accident and concomitant ruptured appendix were the important factors in four cases. In the fifth (a patient admitted in acidosis with 4-plus glucose and 3-plus acetone) perforation of the gallbladder had occurred with an extensive contiguous pathological state. In this one case only could severe diabetes mellitus be said to have been important and, even here, the factor of acute gallbladder disease with perforation overshadowed that of diabetes itself.

10. *The factor of jaundice* as such can now be evaluated. Mortality rates were highest in those patients having jaundice at the time of operation. (Table 1.) Close analysis revealed, however, that jaundice itself played little part in this series of deaths. Among the forty jaundiced patients, there were eleven deaths with postmortem examination being performed in nine. Table III reveals that four deaths were attributable to major accidents. Two were clearly cardiac deaths. In three cases the acuteness and severity of the inflammatory process were most important. Another case was accounted for by other concomitant serious disease and, lastly, in only one case was the cause of death not clearly explained. Analysis of deaths due to hemorrhage in this series also tends to minimize the traditional rôle of jaundice in this regard. There were five deaths due to massive postoperative hemorrhage, each confirmed at autopsy. Three patients were in the "jaundiced" group but autopsy showed laceration of major vessels in two of these. The site of bleeding could not be found even at autopsy in the third jaundiced case and this was therefore conceivably a death in which the effect of jaundice on the clotting mechanism was extremely important. However, the two remaining "hemorrhage" deaths were in nonjaundiced patients and at autopsy, likewise, the site of bleeding could not be found in one. A major laceration accounted for hemorrhage in the other. If autopsies had not been done, those jaundiced patients, all dying from clinically obvious massive

TABLE III

DEATH CAUSES IN THREE MAIN GROUPS

Chronic Cases without Jaundice

(12 Deaths in 241 Cases)

1. Acute pancreatitis	2
2. Accidental	
a. Duodenal tear	1
b. Common duct injury	1
c. Massive liver necrosis	1
d. Biliary fistula	1
Total	4
3. Cardiac	3
4. Concomitant pathology	
a. Erysipelas	1
b. Ruptured appendix	1
c. Bronchopneumonia	1
Total	3

Acute Cases without Jaundice

(12 Deaths in 55 Cases)

1. Acute pathology with fatal extension	6
2. Cardiac	2
3. Concomitant pathology—(Cancer of lung)	1
4. Accidental	
a. Laceration of venous varix	1
b. Hemorrhage—? Source	1
5. Apparent cerebral accident	1

Jaundice Cases

(11 Deaths in 40 Cases)

(9 Autopsies)

1. Accidental	4
2. Cardiac	2
3. Acute gallbladder pathology	3
4. Concomitant serious pathology	1
5. Questionable "liver" death	1

hemorrhage, would have been described as succumbing to the bleeding "tendency" caused by their obstructive jaundice. Lastly, no bleeding of note was found in any of the remaining six jaundiced patients who came to autopsy, while the twenty-nine jaundiced patients who survived operation showed no bleeding during their hospital courses. (Prothrombin studies were not done.) These facts lead to the conclusion that, at least in this series of cases, jaundice as such was not a death factor of great importance.

III. THE LIVING SERIES

A. Complications. Among the living series, the complications encountered are shown in Table IV. As might be expected, when the pathological condition was more acute and progressive, the percentage of complications was higher.

TABLE IV
COMPLICATIONS IN LIVING SERIES

	Chronic	Acute	Jaundiced	Total
1. Postoperative wound infection	18	2	2	22
2. Pulmonary				
a. pneumonitis	9	1	3	13
b. pleurisy with fluid	2	0	0	2
c. atelectasis	2	3	0	5
3. Cardiac				
a. decompensation	1	0	0	1
b. auricular flutter	1	0	0	1
4. Urological				
a. cystitis	2	0	0	2
b. pyelitis	1	0	0	1
c. bladder paralysis	0	1	0	1
5. Biliary fistula	2	1	0	3
6. Evisceration	1	0	0	1
7. Subdiaphragmatic condition	1	0	0	1
8. Suppurative parotitis	1	0	0	1
9. Postoperative psychosis	1	1	0	2
10. "Stormy"	1	3	3	7
Complications—per cent.	19	25	29	

B. Follow-up Study. 1. Table V is a summary of *the clinical results* obtained by gallbladder surgery among the 302 patients of the "living series." It should be explained that the terms excellent, good, fair, etc., are entirely subjective evaluations. The justification for their use exists in that a single observer interviewed and examined a great majority of the patients. A uniform standard of values was thereby attained with error of constant nature. The group of "excellent" and "good" results included patients who had, at follow-up clinic, complete or almost complete relief of all the symptoms they complained of before operation. Restoration of a patient's economic status by a good operative result was taken into account. The "poor results" group included those patients who had many and sometimes all of the symptoms that were present before operation. Table V indicates that improvement followed operation in most instances. The mortality rate was parallel to the degree of improvement in each group, that is, the higher the mortality rate the better were the results in those patients who survived.

2. *Analysis of the Poorer Results.* During the interviews, the impression was obtained that most of the poor results are associated with less definite or minimal disorders. This led to a comparative study of the conditions found in the two major groups, that is, the group of "excellent and good" results and that of "poor" results. The study was based on the reports of the gross and histological pathological status and on the *x*-ray studies of the gallbladder by cholecystogram. The pathological changes were classified as "definite" and "minimal." The latter included minimal stages of gallbladder disease with thin walls, few or no stones and minimal microscopic findings. It was found that in the group of patients with "excellent—good" results, only 5 per cent had "minimal" gallbladder disorders, while 65 per cent in the group of patients with poorer results had minimal changes. Minimal findings were also present in eleven other cases for which no follow-up report was available. On an *x*-ray basis, a similar distinction was made between cases having what were called "definite" and those having "indefi-

TABLE V
RESULTS

Type	Survived	Excellent—Good		Fair		Poor		Mortality Rate, Per Cent
		No. Cases	Per Cent of Patients Returned	No. Cases	Per Cent of Patients Returned	No. Cases	Per Cent of Patients Returned	
Chronic no jaundice	229	145	86	10	6	13	8	4.9
Acute no jaundice	44	37	100	0	..	0	..	21.4
Jaundice at operation	29	24	100	0	..	0	..	27.5

nite" findings. By "indefinite" is meant that group which even in the presence of one or more stones, nevertheless showed some gallbladder function. These *x*-ray reports read "good concentration with poor emptying" or "stone—no impairment of function" or "good emptying—slow filling" or "only slight impairment of gallbladder function." Classed as "definite" were those cases showing absent gallbladder function, with or without visualization of stones. It must be emphasized here that in this study the presence of gallbladder disease of some degree was accurately revealed by the *x*-ray in over 97 per cent of the cases and that this division of *x*-ray reports into "definite" was a purely arbitrary one made in the attempt to understand the poor results. The "indefinite" *x*-ray diagnosis was much more common in the group of "poorer" results.

Both these demonstrations of the effect of minimal changes in morphology and function were confirmed in the more detailed study of thirteen cases in which the results were classed "very poor." In this group, ten of the thirteen patients had "minimal" findings reported and nine of eleven had the "indefinite" type of *x*-ray report. The presumption exists that the basic cause for the poor results is found in the failure to remove the disease process causing the symptoms. Carter et al.[1] arrived at this identical conclusion.

3. The rôle of cholelithiasis in the results is shown in Table VI. While the death rate and the complication rate were slightly higher in those patients having stones, the results were definitely better once the patient survived.

TABLE VI
RÔLE OF CHOLELITHIASIS IN RESULTS

	No Stones 90%, Per Cent	Stones 10%, Per Cent
Death rate	6.8	10.4
Complication rate	13.0	19.0
Results (per cent of total cases)		
a. No trace	34.0	20.0
b. Excellent—good	46.0	64.0
c. Fair	3.0	3.0
d. Poor	6.0	1.3
e. Very poor	3.0	.3

C. "Early" versus "Late" Operation in Acute Gallbladder Disease. There has been much written concerning early versus late operation in the acutely inflamed gallbladder. Pleas have been made for both "early" and "late" surgery. In this study, instead of choosing an arbitrary time limit as to what should be called "early" or "late" operation, the acute cases were divided into two groups depending upon the reason for operation. (Table VII.) Group 2, consisting of thirty-two cases, happened to include patients operated upon from the seventh to seventy-seventh hospital days, with normal temperature, when the acute process was considered to have subsided enough to make operation safe. Group 1 included twenty-eight patients operated upon between the first and fifth hospital days, usually because of

mistaken diagnosis (sixteen cases). These, with four patients operated upon because of an acute condition of the gallbladder requiring intervention and eight others operated upon because of continuing fever and jaundice, served as an effective control "early" group with which to compare the results of "late" operations. Table VII shows that the earlier group had a much higher death rate, with not much difference as to whether cholecystectomy or cholecystotomy had been done. If the patients survived, however, end results in both "early" and "late" groups were about the same. Carter et al. give as their experience the best results in the group "early" surgery, not exceeding twenty-four hours.

TABLE VII

TIME OF OPERATION VERSUS RESULTS ALL ACUTE CASES

	Cases
1. Group one (1–5th day)	28
Operated because of	
a. Mistaken diagnosis	16
b. Acute condition	4
c. Continuing fever or jaundice	8
2. Group two (7–77th day)	36
Operated because of normal temperature (cholecystostomy)	12

	Group One, Per Cent	Group Two, Per Cent
Death rate	32	13
Cholecystectomy	30	4
Cholecystostomy	33	33
Survivals		
a. Complication rate	26	25
Cholecystectomy	16	16
Cholecystostomy	10	9
b. Good results	93	83

Attention is drawn to the fact that in Group 2, which includes all patients with normal temperatures, ostensibly "cooled off," the condition was nevertheless sufficiently severe and acute to require cholecystostomy in twelve of thirty-six cases, with attendant higher mortality. This leads to one of the most instructive facts revealed by this study, namely, that these cases of acute cholecystitis, although subsiding, had not been allowed to subside enough, even though seventy-seven days had passed in the longest case. All of this group were reported as acute by the pathologist or surgeon. This indicates that it would be preferable, once the temperature has become normal, to allow a longer interval, several months, for complete subsidence under careful supervision. Acute cases would thus fall properly into the group of "chronic gallbladder disease without jaundice," with its lower mortality rate. Should an acute flare-up again occur the case could then be treated as an acute attack in whatever way thought best.

D. Gallbladder Disease in the Male. Comparison of the males and females throughout all phases of the study showed that male patients were generally older, they developed the severe acute type of disease more often and their complication and mortality rates were higher. Operative relief was obtained in about equal proportions in both sexes.

E. Problems in Differential Diagnosis. One of the most significant aspects of this surgical study is found in the problems of differential diagnosis encountered.

The carcinomas of the gallbladder and the pancreas numbered thirty. These led to confusion mainly because of the occurrence of obstructive lesions of the common duct. An interesting feature of this group, however, was the existence of advanced disease before obstruction appeared. The patient usually exhibited marked weight loss, large liver and multiple palpable abdominal masses, all of which were found very rarely in the entire surgical group in this study.

The diagnosis of acute appendicitis was erroneously considered eleven times and prompted emergency surgery for appendicitis six times. One case was diagnosed acute cholecystitis and was found to have a ruptured appendix at autopsy.

The clinical picture of *chronic* cholecystitis and cholelithiasis with the finding of advanced severe *acute* condition of the gallbladder at operation occurred five times. In each instance, the patient had a normal temperature. This parallels the finding already stressed of the high inci-

dence of acute, severe, inflammatory disease in patients operated upon after considerable periods of observation in the hospital for supposed complete subsidence of an acute attack. Mentzer[2] stressed this same masquerading of acute gallbladder disorders under various guises. The converse picture of acute disease clinically with the findings at operation of chronic disease occurred only once in our series.

A pathological condition of the right kidney was considered in ten cases to the extent of retrograde urography in seven. Two patients actually turned out to have renal disease and in one it was the only cause of the patient's symptoms. This association has been recently emphasized by Derrah and Kaufman.[3]

Among problems less frequently encountered, chronic peptic ulcer occurred three times. It is of interest that chronic ulcer was palpated at operation in two instances in the entire series. Acute pancreatitis, angina pectoris, coronary occlusion, carcinoma of the stomach, lobar pneumonia, arsenical hepatitis, incarcerated hernia and right diaphragmatic pleurisy cover the range of other conditions considered before operation.

IV. A GROUP OF INTERESTING CASES

Case I. This patient was a seven-year old, white male who was admitted to the Contagious Disease Pavilion of the hospital with the typical history and findings of scarlet fever. On the third hospital day, abdominal pain and tendernesses over McBurney's point led to the diagnosis of acute retrocecal appendicitis. At operation, an acute empyema of the gallbladder was found with impending gangrene. No stones were present. A cholecystostomy was done and the patient had an uneventful postoperative course.

Case II. This patient was a forty-one year old, white male, who died on the medical ward after a short illness of about three weeks, with the classical history, physical findings and laboratory evidence of typhoid fever. At autopsy, in addition to typhoid ulcers of the bowel, the gallbladder was the seat of phlegmonous cholecystitis without stones, confirmed by microscopic examination.

Case III. This patient was a forty-two year old, white female admitted for intense jaundice of five days' duration and severe colicky, right upper quadrant pain radiating to the back and right shoulder. At operation, the common duct was found to have been completely obstructed by multiple ecchinococcic cysts measuring 2 to 3 cm. in diameter. The parasitic nature of these cysts was confirmed microscopically by the finding of typical hooklets and scolices. Postoperatively, the patient continued to discharge smaller cysts through her T tube. She signed out at her own risk in poor condition, was reoperated upon at another hospital and died. No autopsy was obtained.

Case IV. This patient was a fifty-nine year old white male, who had an exploratory laparotomy for intense jaundice of several weeks' duration. The patient had a steadily downhill postoperative course. Postmortem examination revealed a scirrhous carcinoma of the body of the pancreas. Normal pancreatic tissue intervened between the tumor and the common duct. The latter, however, was the site of an independent primary carcinoma, which had produced complete obstruction.

Case V and VI. These are two cases of bronchial asthma in which marked and dramatic but only temporary relief from asthmatic attacks was noted following the removal of chronically infected gallbladders.

Case VII. Finally, there is mentioned the case of a sixty-two year old, white female, who had what was supposed to have been a cholecystectomy twenty years previously. She was admitted with a large herniating mass in the region of her operative scar thought to be incarcerated bowel. Operation revealed the hernial sac to be completely filled by a tremendously dilated, chronically infected gallbladder containing many stones.

SUMMARY

Five years of gallbladder disease at a general hospital were reviewed with a study of 337 surgical cases.

1. The mortality rate is lowest in the "chronic without jaundice" group and highest in those patients jaundiced at the time of operation.

2. Those cases in which death occurred were, in general, of an emergency nature.

3. The causes of death may be summarized briefly: (a) The cardiac factor was

important in nine deaths; (b) the accidental factor was important in ten deaths; (c) other concomitant serious pathological conditions were important in three deaths; (d) acute severe conditions of the gallbladder accounted for seven deaths and perforation played an important part; (e) the chronicity of the disease contributed to the death total by causing acute pancreatitis, marked hepatitis and jaundice; (f) jaundice was not an important death factor in this series; and (g) gallbladder disease as such accounted for death most frequently in the acute type of case.

4. Results in general were good. Poor results were associated with less definite findings, both pathologically and by *x*-ray.

5. In acute cases, "early" operations were attended by a higher mortality rate than "late" ones.

6. Many gallbladders, "cooled off" and thought to have subsided, still showed acute conditions at operation.

7. The male patient was usually older and had the more acute type of disease, with higher complication and mortality rates than the female.

8. Some problems in differential diagnosis are discussed.

9. A group of unusual cases is presented.

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FIVE YEARS OF GALLBLADDER DISEASE AT AUTOPSY IN A GENERAL HOSPITAL*

A REVIEW OF 2,450 CONSECUTIVE ROUTINE AUTOPSIES

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THE object of this study was to note the incidence and nature of gallbladder disease as found in a large series of consecutive routine autopsies at a general hospital. The bed capacity of Queens General Hospital is 700 and the average hospital stay is nine days. Annually, the autopsy percentage has been consistently over 58 per cent and as high as 66 per cent, with an average of 500 house autopsies done each year.

I. INCIDENCE OF GALLBLADDER DISEASE IN ROUTINE AUTOPSIES

Medical literature contains many studies done in the past noting the incidence of gallstones among routine autopsies. (Table I.) In the present study (Table II), the total number of routine autopsies was 2,450, covering a five-year period between November, 1935, and November, 1940. Cases of cholecystitis with or without cholelithiasis numbered 271. The gross incidence for the entire series was 11 per cent. Corrections for age groups are also shown in Table II. The rising incidence in older subjects is noteworthy. One in every five patients over sixty years of age was found to have cholecystitis or cholelithiasis, regardless of the cause of death.

TABLE I
INCIDENCE OF GALLSTONES IN ROUTINE AUTOPSIES

Author	No. of Autopsies	Per Cent Incidence
Munich (Ritter)	19,974	7.8
Petrograd (Hesse)	17,402	2.1
Basle (Roth)	16,025	10.7
London (Ticehurst)	11,133	3.0
Copenhagen (Paulsen)	9,172	3.8
Japan (Miyake)	8,406	3.0
Kiel (Peters)	5,962	2.7
London (Rolleston)	4,616	5.8
Calcutta (Rogers)	4,544	5.3
Dresden (Fiedler)	4,300	6.3
London (Walton)	3,775	3.4
Sweden (Scheel)	2,753	15.0
New York (Hertes)	2,371	7.6
Gottingen (Hunerhoff)	1,951	4.4
Albany (Stanton)	1,667	7.2
Baltimore (Mosher)	1,665	6.9
Chicago (Mitchell)	1,600	3.1
Manchester (Brockbank)	1,347	7.4
Strasbourg (Shroeder)	1,150	1.2
Panama (Clark)	1,088	2.2
Tomsk (Hesse)	1,000	2.1
Toronto (Ryerson)	333	4.0
Recent Reviews		
Mentzer (Mayo Clinic) 1926	612	21.0
Crump (Vienna) 1931	1,000	32.0
Ludlow (Cleveland) 1937	4,800	7.0

II. THE PATHOLOGICAL CONDITIONS ENCOUNTERED IN THE GALLBLADDER

Gross and microscopic criteria were used. Microscopic examinations had not been done in all of the routine cases, when the gallbladder appeared "normal," or had obvious gross disease. One hundred consecutive cases current during 1940 were studied to serve as a control group. Four gallbladders grossly "normal" showed some degree of round cell infiltration on microscopic study. Two of these, in addition, had moderate interstitial fibrosis. In ninety-six cases, a gross diagnosis of "normal gallbladder" was confirmed microscopically.

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Findings in the gallbladder fell easily into two major groups: The first including only uncomplicated cholecystitis with or without stone totalled 271 cases. In the second group were all other types of gallbladder conditions not considered in the calculation of the 11 per cent incidence.

TABLE II
INCIDENCE OF CHOLECYSTITIS IN 2,450 ROUTINE AUTOPSIES AT QUEENS GENERAL HOSPITAL

Age Group	No. of Cases	Cases of Gallbladder Disease	Per Cent Incidence
All ages.....	2450	271	11.0
Under 2 yrs.....	340	0	0.0
2–10 "	98	0	0.0
10–20 "	95	2	2.0
20–30 "	176	7	4.2
30–40 "	220	13	6.3
40–50 "	343	38	11.0
50–60 "	450	59	13.5
60–70 "	412	79	19.0
70–80 "	257	58	22.0
80–90 "	58	15	25.0

Age Group	Per Cent Incidence
All patients over 40 yrs.....	15.0
" " " 50 "	18.0
" " " 60 "	20.0
" " " 70 "	22.0
" " " 80 "	26.0

In the *first group* (cholecystitis with or without stones), the extent of inflammatory involvement of the gallbladder was found variable but permitted of further subdivision into three principal subgroups: (a) severe involvement (acute and chronic); (b) moderately advanced involvement and (c) minimal involvement. These three types were about equally distributed among the various age groups. (Fig. 1.)

(*a*) The *severe acute* disease encountered varied from diffuse exudative cholecystitis to empyema of the gallbladder with perforation. There were fourteen such cases, eight males and six females. Although this is a small series, this finding differs from the generally accepted idea that severe acute gallbladder disease is more common in the female. Nine of these fourteen severe acute cases had progressed to empyema of the gallbladder, each with associated cholelithiasis. Perforation occurred in seven of the nine empyemas and was directly responsible for death in five cases. Regional abscesses, multiple fistula formation and generalized peritonitis followed perforations and accounted for these mortalities. The remaining two patients with perforation died of sepsis from other causes (infected leg varicosity and ruptured colonic diverticulum). The two patients with unperforated empyema died nevertheless of their gallbladder disease with sepsis an important factor.

Acute inflammatory changes other than empyema included an acute diffuse exudative cholecystitis in a patient who died of subacute nephritis, an instance of focal suppuration in a chronically inflamed gallbladder wall, two cases of acute phlegmonous cholecystitis in postabortal and genitourinary sepsis and one case of gangrenous cholecystitis in a patient who died of fulminating typhoid fever. The occurrence of diffuse exudative cholecystitis in sepsis is of considerable theoretical as well as practical interest. Seeding of bacteria from the blood stream into the gallbladder walls, with subsequent progressive acute inflammation is strongly suggested. Seven of the fourteen patients with the severe acute type of gallbladder disease succumbed to it. The others died of various other causes.

Severe chronic inflammatory changes were present in fifty-six instances. Thirty-seven of these presented marked contraction and thickening of the gallbladder wall, with many stones but no obstructive condition in the biliary ducts. There were, in addition, fifteen cases of hydrops of the gallbladder, with chronically thickened walls, clear fluid, impacted calculi in the cystic duct and little other contiguous change. Only one death in this entire group of fifty-six cases could be attributed

directly to a pathological condition of the gallbladder.

(*b*) *Moderately advanced pathological changes* were found in forty-five instances.

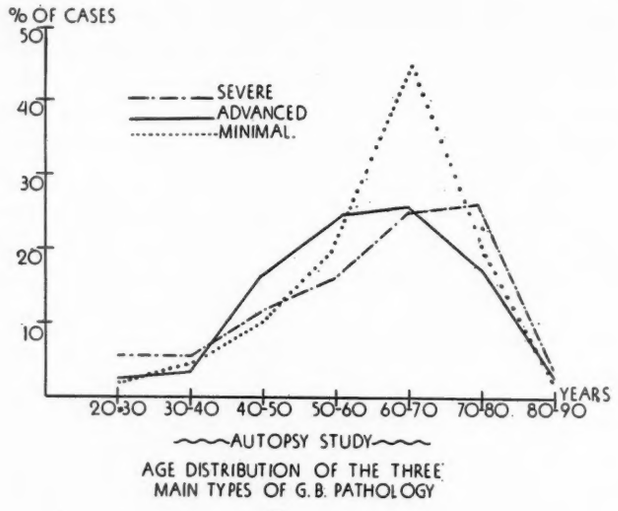

FIG. 1.

Here the gross changes were less marked than in the "severe" type, with less thickening of the walls, fewer stones and usually intact mucosa. Microscopically, there was definite but not marked round cell infiltration and fibrosis. Males numbered twenty, females twenty-five, in this group and cholelithiasis was present in 80 per cent of cases. None of these patients died of his gallbladder disease.

(*c*) *Minimal pathological changes* were found in 156 instances, the great majority. Here females outnumbered males, ninety-five to sixty-one. Cholelithiasis was present in 80 per cent of cases. Minimal thickening of the wall with intact mucosa and only one or more small stones were usually present. No deaths were attributable to gallbladder disease in this group.

CLINICAL CORRELATION

A positive history of recognizable symptoms referable to the gallbladder was elicited in only thirteen of the 271 cases found to have gallbladder disease at autopsy (4 per cent). Only five of the seventy cases of severe disease, one of the forty-five moderately advanced cases and seven of the 156 minimal disease group had a positive history. Symptoms varied from slight belching after meals to severe attacks of right upper quadrant pain.

Non-inflammatory changes in the gallbladder, not included in the 11 per cent incidence, composed the *second major group* which included the following: Carcinoma of the gallbladder was found eight times and was associated with cholelithiasis four times. Cholesterolosis was present in sixteen cases. Miscellaneous conditions included leukemic infiltration (two), mucosal polyps (three), acute "uremic" ulceration (one), adenomyoma (two), marked edema of the entire wall in chronic passive congestion (two), metastatic carcinoma (two) and miliary tuberculosis (one).

III. ASSOCIATED PATHOLOGICAL CONDITIONS ENCOUNTERED

Obstruction by stone was the most frequent *biliary duct* lesion associated with cholecystitis. In the common bile duct, this occurred in nine instances. In the cystic duct, it occurred in fifteen cases of hydrops and in nine cases of acute empyema of the gallbladder.

Abnormal dilatation of the common bile duct was found in ten cases. In four of these, cholecystectomy had been done, and cholelithiasis was present in six. This

dilatation may have represented the effects of stones previously passed.

Postinflammatory stricture of the common duct was noted in two cases.

Carcinomatous obstructions of the biliary ducts were numerous, but the great majority were not associated with intrinsic gallbladder disease. The common hepatic duct was the seat of primary carcinoma in three and the right hepatic duct in one. Common bile duct obstruction by cancer occurred twenty-eight times, with primary sites in the pancreas (twenty-two); in the prostate (one); in the gallbladder (three) and in the rectum (one) and stomach (one). Only one case of primary carcinoma of the common duct was found. It is to be emphasized that the obstruction of the common duct was due to actual invasion of the duct wall in almost every instance. Direct extension of tumor tissue from adjacent lesions resulted in annular stenosing constrictions of the common duct or in an obstructive intraductal lesion, often with ulceration of the duct mucosa. Rarely was compression of the duct by surrounding tumor tissue the mechanism of obstructive jaundice in these cases.

The *liver* lesions encountered in the group of patients with gallbladder disease were seen to be of a type predominantly unrelated to gallbladder disorders. *Biliary cirrhosis* was seen only five times in the entire series of 271 cases, an incidence of 2 per cent. It occurred only in the severe disease group, associated with severe acute inflammation in three cases. In the moderately advanced and minimal disease groups it did not appear at all. There were two cases of obstructing malignancy in the common duct, however, which did have accompanying marked biliary cirrhosis. The "Laennec" type of cirrhosis was found, independently, much more frequently throughout the series. *Cholangitis* occurred only ten times in the entire series (3.8 per cent). Five cases of severe acute gallbladder disease and three of severe chronic type had associated cholangitis. There was no cholangitis in the moderately advanced pathological group. In two instances of minimal gallbladder disease, cholangitis was present. One of these patients died of meningitis, the other of malignant obstruction of the common duct. Cholangitis was seen to be of more marked degree when obstructive jaundice was present, which occurred in five of the ten cases.

Some of the other liver lesions encountered in these 271 patients with gallbladder disease were; chronic passive congestion, five; fatty change, thirty-four; round cell infiltration into portal areas, twenty-nine; of marked degree, three; metastatic carcinoma, all sources, twenty-six; fibrosis, nineteen; marked, one; Laennec's cirrhosis, twenty-two; bile stasis with jaundice, eight; multiple abscesses, seven; diffuse hepatitis, five (not gallbladder cases); focal necrosis in presence of sepsis, five; miscellaneous lesions including hemangioma, miliary tuberculosis, hepatomá and Hodgkin's disease.

Lesions of the *pancreas* as of the liver did not seem to be significantly related to gallbladder disease in this autopsy series. "Interstitial fibrosis" was the most common lesion, occurring forty-three times, but was of marked degree only five times. There was no demonstrable relationship between the severity of the gallbladder disease and the degree of fibrosis. Chronic pancreatitis was observed in nine instances, 4 per cent. Severe gallbladder disease was present in five of these. Acute pancreatitis was observed in only one case of gallbladder disease, classed "severe." It was seen once each in a case of carcinoma of the common hepatic duct and in a carcinoma of the gallbladder neck with impacted cystic duct stone.

Disease of the *appendix* showed no demonstrable relationship to gallbladder disease. Previous appendectomy was noted sixteen times. Ruptured appendix causing fatal peritonitis occurred in three cases. Appendiceal fibrosis was observed in three cases and mucocoele of the appendix in one.

IV. THE RELATIONSHIP OF GALLBLADDER DISEASE TO ARTERIOSCLEROSIS

There has been much written concerning the difficulty often met in distinguishing an acute gallbladder attack from an acute coronary occlusion or spasm. The material here reviewed offered an excellent opportunity for investigation of the association between arteriosclerosis and gallbladder disease on a firm pathological basis. For this purpose, patients *with* gallbladder disease and patients in similar age groups *without* gallbladder disease were compared. A study was made of the arteries in the 271 cases of gallbladder disease and in a large control group of 1,045 patients. The degree of arteriosclerotic change in the coronary, renal and cerebral vessels and in the aorta was noted. The results are tabulated in Table III. "Marked changes" include widespread atheromatous involvement of calcification, and in the coronaries, any recent or old occlusion. In the interpretation of "moderate" changes, the personal equation of the pathologist entered, but this entire series of autopsies was done under uniform supervision and the number was large enough so that the margin of error is small. The renal lesions were interpreted mainly on microscopic grounds. Lesions taken to be of the greatest significance were those in the coronary arteries.

The conclusion arrived at as a result of this study was that arteriosclerosis generally and marked coronary disease specifically are not more common or present in severer degree in patients with gallbladder

TABLE III

ARTERIOSCLEROSIS STUDY

Patients with Marked Coronary Sclerosis			Patients with Gallbladder Disease	
Age	Patients without Gallbladder Disease, Per Cent	Patients with Gallbladder Disease, Per Cent	Degree of Gallbladder Disease	Per Cent Marked Coronary Sclerosis, Per Cent
Over 50	28	30	Severe	30
Under 50	18	5	Moderate	20
			Minimal	20

Table in Full

	271 Patients with Gallbladder Disease (All Ages)				1045 Patients without Gallbladder Disease (All Ages)			
	Coronary, Per Cent	Kidney, Per Cent	Cerebral, Per Cent	Aorta, Per Cent	Coronary, Per Cent	Kidney, Per Cent	Cerebral, Per Cent	Aorta, Per Cent
Over 50 (214)					(910)			
Marked	30	6	21	21	28	6	16	21
Moderate	28	32	18	18	24	9	20	39
Minimal	42	62	61	69	48	85	64	40
Under 50 (57)					(135)			
Marked	5	3	3	8	18	5	12	16
Moderate	18	17	3	18	28	15	15	37
Minimal	77	80	94	74	54	80	73	47

disease. Confirmatory evidence was found in that deaths of a vascular type, namely, those due to arteriosclerotic gangrene of the extremities without diabetes, arteriosclerotic heart disease with failure, cerebral hemorrhage and directly allied conditions were not more common in the group with gallbladder disease than in the control group.

These findings coincide with those of Tennant and Zimmerman[4] who analyzed 1,600 consecutive autopsies. They concluded that "there is no significant association in the occurrence of gallbladder disease and arteriosclerotic heart disease in an age period in which most of the instances of each lie."

SUMMARY

Gallbladder disease in 2,450 consecutive autopsies during a five-year period at a general hospital were reviewed:

1. "Incidental" gallbladder disease with stone was found in 271 cases (11 per cent). With each decade this figure increased, reaching 25 per cent in the eighth decade. Symptoms referable to the gallbladder had been elicited in only 4 per cent of cases.

2. Seventy (25 per cent) of the 271 cases of gallbladder disease were "severe" in degree. Severe, acute pathological conditions accounted for the highest percentage of "gallbladder deaths," and perforation played a predominant rôle. Severe chronic disease was manifested principally by cases of hydrops of the gallbladder and of marked contracted chronic cholecystitis and cholelithiasis. Only one death was due to "gallbladder disease" in this group. Only five of seventy patients who showed severe gallbladder disease at autopsy showed any clinical symptoms referable to the gallbladder.

3. Moderately advanced and minimal gallbladder conditions comprised 16 per cent and 59 per cent, respectively, of the entire series and accounted for no deaths.

4. Obstruction by stone was the most common lesion of the biliary ducts associated with cholecystitis in this series. The "invasion" mechanism of carcinomatous obstructive jaundice is emphasized.

5. Inflammation of the gallbladder gave rise to few instances of liver disease in this series. Biliary cirrhosis and cholangitis occurred in a relatively small number of cases.

6. Pancreatic disease resulting from acute or chronic gallbladder disease was not found frequently.

7. No appendiceal abnormality of any significance in relation to gallbladder disease was found.

8. Coronary sclerosis and general arteriosclerosis are not significantly more common among patients with gallbladder disease.

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THE IMPONDERABLES IN GENITOURINARY CARCINOMA

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DURING the past two years I have seen three patients originally suffering from genitourinary carcinoma, whom I believed to be dying of the primary carcinoma or its metastases. They looked cachectic, had lost much weight, had grave, unbearable pain and had every appearance of an early demise. All these patients had intraspinal absolute alcohol injections to control their pain.

All three of these patients are comparatively well now. Two have survived approximately five years after first seen, and I believe have no malignant disease. The remaining one is still in the doubtful class as far as final control of his disease is concerned. The history of these three cases is as follows:

CASE REPORTS

CASE I. A. F. W., age twenty-four years, was admitted to the Memorial Hospital on November 30, 1937, with the following history: Two months prior to entry he noticed a painless swelling of the left testicle. An Aschheim-Zondek test at that time was negative. The patient was given thirty *x*-ray treatments to the testicle and the left quadrant. The testicular tumor increased somewhat after these treatments. The patient had a dull pain in the left lower quadrant. He lost about ten pounds in weight within a month.

Physical examination revealed a sharp *x*-ray reaction to the skin on the lower quadrant. The right testicle was atrophic and the left testicle the size of a large lemon. The skin of the scrotum was desquamating. The Aschheim-Zondek test was again done and this time showed 500 prolan A and 100 prolan B. Later the prolan B increased to 200. There were masses felt in his abdomen and left supraclavicular region. A film of his lungs was not taken at this time. Following this *x*-ray therapy was given between December 16, 1937, and January 21, 1938. He received 1,500 R to the left testicle at a distance of 50 cm., 1,800 R at a distance of 70 cm. was given to each of four portals of entry: left lower quadrant anterior, left lower quadrant posterior, left upper quadrant anterior, left upper quadrant posterior. This had no affect on the size of the testicular tumor. An orchidectomy was done on February 3, 1938, under spinal anesthesia.

The pathological examination of the tumor showed embryonal adenocarcinoma Grade III. The testicle was partially necrotic but there was much fully viable disease. On April 27, 1938, there was observed a left supraclavicular gland metastasis. A picture of his lungs at this time showed no metastases. His left lower neck and his upper and lower mediastinum were given deep *x*-ray therapy. On June 28, 1938, he complained of severe pain along the course of the right sacral nerve and was believed to have metastasis here. The right sacral nerve was treated with deep *x*-ray therapy 1,200 R anteriorly and 1,200 R posteriorly with portals anterior and posterior at a distance of 50 cm. This treatment did not affect his pain and he began to take codeine. He had lost a good deal of weight and was considered to be in a serious condition. He finally was taking about ¼ gr. every four or five hours for pain relief. His weight was about 135 pounds. He looked very badly, cachectic and it seemed as if he were soon to succumb from his disease. Because of his pain he was given cobra venom injections and he received twenty-one injections of 1 cc. each between February 16, 1939, and March 15, 1939. This gave him some relief but on the whole was ineffective.

His main symptoms were severe pain along the course of the right sacral nerve, general cachexia and great loss of weight. He was given an intraspinous alcohol injection of 12 m. between the last dorsal and first lumbar vertebra. His pain disappeared almost immediately. On June 27, 1939, he reported a gain of some forty-five pounds in weight, he had no pain and had returned to work. On October 26, 1939, he had gained fifty-nine pounds in weight. There was some thickness of the left supraclavicular area. In February, 1942, his

condition was excellent; there was no sign of disease and the patient was working.

Comment. This patient's symptoms were apparently due to pressure upon the left sciatic nerve by tumor which was being changed by deep roentgen therapy into scar tissue. His pain and the sedatives he had to take in the attempt to control the pain gave him every appearance of carcinomatous cachexia. I believe he would have died if his pain had not been controlled.

Case II. J. S. was first seen at the Memorial Hospital on May 12, 1937, with a history of one and one-half years of profuse hematuria without pain. On September 1, 1936, a tumor of the bladder was removed in an outside hospital. Following this he had some *x*-ray treatment. Six weeks before he was seen he began to have terminal hematuria with urgency, frequency, pain and nocturia but no incontinence. The patient had lost thirty pounds. Cystoscopy showed a large flat ulcerated tumor, very extensive on the left side of the bladder base and the lower left lateral wall. The specimen removed showed "epidermoid carcinoma Grade III." The tumor was considered too extensive for suprapubic implantation of radon seeds. On May 13, 1937, he was treated by surface application of unscreened radium through the cystoscope receiving 749 millicurie hours. He had 20 to 30 cc. residual urine. His condition improved considerably. The radium application caused a good deal of superficial slough of the tumor. He developed a duodenal ulcer and on May 27, 1938, and had a posterior gastroenterostomy from which he recovered. On September 23, 1938, he had a good deal of bladder pain and dysuria, much slough and calcareous material was washed from his bladder. On February 21, 1939, rectal examination revealed much induration of the bladder base and he still had an extensive infiltrating tumor. He was put on deep *x*-ray therapy and from February 21, 1939, to April 27, 1939, he received 1,600 R to four portals of entry: left anterior pelvis, left pelvis posterior, right pelvis anterior, right pelvis posterior, at a distance of 70 cm. from a portal of 11 by 14 cm. From June 27, 1939, to July 13, 1939, he received 450 R to four portals at a distance of 50 cm. From August 15, 1939, to September 23, 1939, he received to each of two portals anterior and posterior 1,000 R at a distance of 50 cm. On March 7, 1939, he had a great increase of bladder spasm and pain. For this pain between March 10, 1939, and March 22, 1939, he was given ten injections of 1 cc. each of cobra venom. This did him little good.

On March 23, 1939, he entered the hospital and was given an intraspinous injection of 12 m. of absolute alcohol. The patient was placed on the left side and the injection given between the last lumbar and first dorsal vertebra. His pain stopped almost immediately. He gained markedly in weight. There was almost complete absence of pain for six months after the alcohol injection. He still had a moderate amount of hematuria and some dysuria, but it was not enough to indicate another alcohol injection. On June 28, 1940, the patient was in excellent shape; there was some incontinence particularly at night, moderate urinary frequency and a lack of sphincter control when the patient was on his feet. He had gained weight. In January 1942, he was free of pain but had urinary frequency. No tumor could be detected through the cystoscope. He had several areas of white slough in the bladder.

Comment. This patient apparently was dying from his carcinoma during the course of treatment by radiation therapy. Alleviation of his pain turned the tables and gave the radiation therapy a chance to complete its control.

Case III. H. L. L., age sixty-five years, was admitted to the Memorial Hospital on October 21, 1940, with a history of having had a bladder carcinoma, which had been treated at another hospital six months before by means of suprapubic implantation of radon seeds. Subsequent to this he was confined to bed. He had lost a large amount of weight. He looked cachectic. The patient was passing some of his urine through the suprapubic opening and was constantly dribbling the remainder through his urethra. The suprapubic area was widely indurated either from infection or from carcinoma, I could not tell which. Rectal examination revealed massive periprostatic induration which likewise was either caused by extensive tumor growth beyond the bladder or inflammation. Under spinal anesthesia he was cystoscoped. The bladder was filled with white slough. With the stone evacuator very large quantities of slough covered with calcareous deposits were removed from his bladder. His suprapubic wound healed completely in two

days. His incontinence ceased but he had a great deal of pain in urinating. On November 20, 1940, intraspinous alcohol injection of 12 m. was given between the last dorsal and first lumbar vertebra in the right side. On November 25, 1940, as the first injection had not entirely controlled his pain, the second injection of 14 m. of alcohol was intraspinously injected on the left side. This entirely controlled his pain. He began immediately to improve, got out of bed and went home. By February, 1942, he had gained about twenty pounds in weight and looked well. His urine was cloudy with pus. He was incontinent by day. His periprostatic induration had almost disappeared. He had had no hematuria and I believe his bladder carcinoma has been controlled.

Comment. This patient obviously was suffering from massive slough formation and infection. Removal of the slough and controlling his pain gave him a chance to get well.

These three cases are in the class of imponderables in genitourinary carcinoma. With just a shade of casualness in estimating the real underlying cause of their condition, with the usual methods of combating their pain, morphine, etc., all three might easily have died not of their carcinoma but of attendant and unexpected complications. If the patients' pain had not been controlled by the intraspinous alcohol injections, two of them, I believe, would surely have died.

The explanation of the recovery of the third patient is comparatively simple. He had massive slough and stone formation of his bladder caused by radium implants. These caused severe infection of his urinary tract. Removing the stones from his bladder controlled the infection.

The explanation of the recovery of the two other patients is not as simple. The patient with teratoma testis must have had perineural metastasis as a cause of his pain. His pain alone was causing his physical deterioration and I believe would have caused his death. His subsequent rapid recovery when his pain ceased, his all around physical improvement gave the roentgen therapy, which he previously had, a chance to complete its ultimate destruction of the metastatic teratoma.

This perhaps implicates a new and previously unsuspected principle in the treatment of intractable and extensive carcinoma. Deep *x*-ray therapy has proved singularly inadequate in controlling many body cancers in spite of the persistent endeavors of the best cancer-minded physicians of the entire world. It has been so nearly adequate and yet it has failed.

I think everyone agrees that the obliterating endateritis in the tumor vessels caused by deep *x*-ray treatment is a much more important effect than the primary and early cell destruction. The former is, however, a long distance effect. It takes a long time, months even years.

In most cases the race between the growth of the cancer and the healing *x*-ray has been a very unequal one. The cancer has nearly always won out. In addition to the cancer growth *per se* causing bodily destruction and finally death we have long known that infection of the cancer and of organs adjacent to the cancer very materially adds to the bodily disintegration. This is especially true in some internal cancers e.g., bladder and cervical cancers. In these two the destructive effect of the infection of the bladder and kidneys may catch up with and pass that of the original cancer.

To this destructive effect of infection must be added in at least some cases the destructive affect of *pain*. This is clearly shown in Cases I and II above reported. The control of pain releases this destructive affect and certainly gives the deep *x*-ray therapy a longer and more propitious chance to get in its work.

We have had fourteen cases to which we have given intraspinous alcohol injections for the relief of pain. All of these patients have been considered dying of their disease. Two of these patients (Cases I and II) have entirely recovered because of the control of pain.

The study of the control of pain in cancer may cause even revolutionary changes in the treatment of such patients.

SUTURE DRESSING ANCHOR

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THE present methods of closing wounds of the skin, whether traumatic or operative incisions, have held for many years and in spite of the means of closure used, not much thought has been given to the objectionable features. Regardless of whether black silk, clips, silkworm gut, wire or other materials are used, all have certain definite points in their favor as well as objectionable features.

After all types of wounds are closed, the usual practice is to place sterile dressings thereon and then secure these dressings in place by means of adhesive tape. The objections to adhesive tape are innumerable. No individual has ever looked back with pleasure upon the time that adhesive tape was removed from his skin, particularly from his abdomen or extremity, taking therewith areas of skin, leaving the tender raw surface exposed to secondary infection. It is always too tight or too loose. It pulls away, denuding the skin under the edges. It is dirty, irritates the skin, itches, or causes blisters and in some persons causes an actual dermatitis in sensitive cases, vesicular or bullous in type.

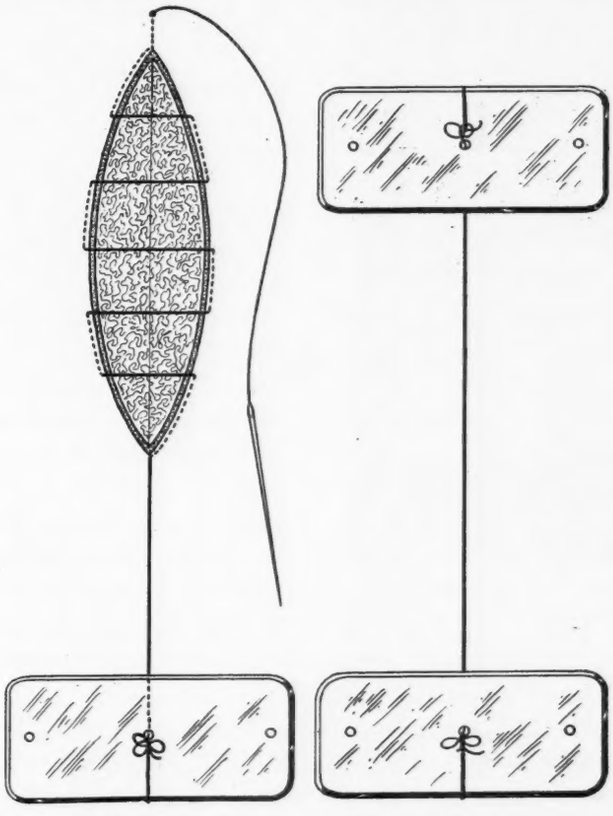

FIG. 1. FIG. 2.

FIG. 1. Incision partly closed with a subcuticular stitch. One suture anchor attached in place, with catgut emerging from under skin beyond incision.
FIG. 2. Incision closed and both anchors attached in place.

All in all, a great deal can be said against our present methods of wound closure and protective dressings. With the multiple bad

features constantly in mind, over a period of years I have attempted many devious ways to avoid these very features. Later,

Fig. 3. Dressings in place, closed and attached to anchors.

in some 100 cases, I have tried a new device in conjunction with the infrequently used subcuticular stitch, a method whereby the wound is closed, the device attached and the dressings attached in their turn to the device.

Many laudatory features can be enumerated in favor of the use of a well placed subcuticular stitch: (1) The subcuticular stitch prevents the making of multiple punctate openings in the skin surface adjacent to the wound, thus obviating multiple points at which infection may occur. (2) It prevents the common occurrence of puncturing superficial blood vessels with subsequent bleeding. (3) It prevents superficial pressure on the wound from sutures or clips too tightly placed with resultant pressure cuts and edema. (4) It offers better approximation of the skin edges and consequently a better cosmetic effect. (5) It removes entirely the painful experience entailed in the removal of sutures or clips with a secondary reopening of multiple avenues of infection.

Before explaining the method in detail it will be well to state at this point that the subcuticular stitch of any fine catgut from No. 0 to 00000 is placed and to the free ends of this are attached the suture dressing anchor as shown in Figure 1. To this suture dressing anchor, sterile dressings are attached. (Figs. 1 and 2.) With the dressings fastened to the anchor no adhesive tape is used. The dressing is in place and remains so (Fig. 3.) Because no adhesive tape is used, the patient is spared the objectionable features enumerated previously against adhesive tape; and in any hospital where this method is used, and even in the physician's and surgeon's office, considerable saving results to the hospital or surgeon from the decrease in the use of adhesive tape and closure materials.

The device is made in various sizes and can be used on any external part of the body from the head to the feet. The same device can be used to place tension sutures and do away with silkworm gut and rubber tubing and their often evil aftermath, edema, tension abscesses and skin inflammations.

Present nonabsorbable skin closure materials and dressing securements are wasteful, painful and should be remedied from the viewpoint of patient, surgeon and hospital.

METHOD

All wounds are closed in the usual manner until all but the skin is left to be closed. At this point one of the suture dressing anchors is firmly attached to the end of a length of fine catgut. The needle is inserted in the skin about ⅜ to ½ inch from either end of the incision. The usual subcuticular stitch is followed and drawn lightly until the edges are approximated, thus closing the wound, until the opposite end of the incision is reached, at which point the needle emerges through the skin surface about ⅜ to ½ inch from the other

end of the incision. At this point the needle and catgut are passed through the center hole of the other anchor. It is threaded through once or twice and then tied in place. Both knots, therefore, are on the upper surface of the anchor and not between the anchor and the skin. Sterile dressings of the required size are next applied by cutting slits at the top and bottom of the dressing just enough to permit the cut ends to be slipped under the anchor at top and bottom, thus covering the wound entirely and the two very small areas of catgut between the skin and the anchor. With the remainder of the catgut, sutures are taken in the dressing to close the two slit ends extending beyond the anchors, and the dressings in turn are fastened to the two lateral holes in the anchor with catgut. The dressing at this point may be considered finished if it is a small dressing on the scalp or face, or any other part of the body; if on the abdomen, an abdominal pad and many-tail binder are applied, or if on an extremity a light gauze or muslin bandage.

In this way the outer dressing may be removed at any time without disturbing the sterile dressing or the anchor itself; in fact the sterile dressing also may be removed and a new one placed at any time.

In clean operative wounds I always leave the original dressing untouched and at any time within five to seven days the dressing will detach itself with the anchors still securely fastened to the gauze, due to the subcuticular digestion of the catgut itself, making a clean, closed and better cosmetic wound.

ABDOMINOPERINEAL OPERATIONS FOR RECTAL AND RECTOSIGMOIDAL CANCER

NEW MODIFICATION OF MILES' TECHNIC FOR DIFFICULT DISSECTIONS

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ABDOMINOPERINEAL resections are the operations of choice for removing rectal and rectosigmoidal cancer. By employing both the abdominal and perineal approach one is able to carry out the widest dissection and provide patients with the greatest possibility of clinical cure. Operations of this nature are ideal for all patients with operable cancers except those in very poor physical condition.

The most satisfactory abdominoperineal operation is the one devised by Miles,[1] of London, in 1907. This operation has stood the test of time and is widely employed today. While there have been a number of improvements in technic since it was originally described, the principles of dissection remain the same. The anus, rectum and lower half of the sigmoid colon are removed, together with adjacent tissues which may contain malignant cells. The patient is left with a permanent abdominal colostomy.

The Miles' operation has been frequently described and need not be repeated in detail. The following is a summary of the more important steps in this operation: The abdomen is opened through a lower left paramedian incision, the rectus muscle being retracted to the left. The abdominal cavity is explored for other tumors of the gastrointestinal tract, extent of the primary tumor, metastatic disease and other abdominal pathological conditions. The dissection is commenced by ligating the inferior mesentery artery; the site of selection is between the first and second sigmoidal arteries. The rectum is freed from the lateral and posterior borders of the pelvis. The lateral leaves of the mesosigmoid and mesorectum are divided after a moderate degree of mobilization of the adjacent pelvic peritoneum. Incisions are carried down parallel to the bowel on either side and connected anteriorly to the rectum. Care must be exercised in ligating the vessels and dividing the pelvic peritoneum on the left side, lest an abnormally located left ureter be injured. The rectum is separated from its anterior attachments, namely, the base of the bladder and seminal vesicles in the male, and the posterior vaginal wall in the female. The separation is extended as far as is convenient; usually it reaches the level of the prostate in the male. The abdominal part of the dissection is completed by cutting the lateral ligaments.

Following pelvic dissection, the sigmoid colon is divided. In recent years this procedure has been greatly facilitated by use of the Zachary Cope or other modifications of the De Martel clamp. The distal segment of pelvic colon and upper rectum are placed in the presacral space and the new pelvic floor is constructed. Construction of the pelvic floor is greatly facilitated by liberal mobilization of the pelvic peritoneum. The proximal end of the pelvic colon is brought through the original incision or through a stab wound to form a colostomy. The gut need not be sutured to the left lateral wall nor need it be sutured to the wound. The wound is closed in layers and a dressing applied.

The final step consists of dissecting free the anal canal and lower part of the rectum through a perineal incision. Miles places the patient on the left side for this part of the operation. Some surgeons turn the patient

on his abdomen, while others including ourselves, prefer the lithotomy position. The feet are placed in stirrups and the buttocks drawn down to the end of the table and elevated by means of a sand bag. The anus is closed with a purse-string suture and the operation completed by wide dissection. Seldom is it necessary to remove the coccyx. After the terminal section of bowel has been dissected free and removed, a rubber glove packed with gauze is inserted into the pelvic cavity, the skin closed with two or three superficial sutures and a dressing applied.

Numerous modifications of the Miles' technic have appeared in the current literature. A number of these modifications have been in the form of two-stage procedures, while others have been completed in one stage. In some instances the perineal has preceded the abdominal dissection. Many of the modifications are being less frequently employed because the advantages of the original abdominoperineal procedure are becoming more generally recognized. After a limited experience with a number of different types of abdominoperineal resections, there appear to be three operations or three slightly different forms of technic which are worthy of consideration: First, the Miles' operation, as previously described; this technic being suitable for the majority of patients; second, a slight modification of the Miles' operation, to be described; this modified one-stage technic facilitates the dissection in certain difficult cases; and third, the Lahey two-stage abdominoperineal resection.

The following technic has been employed in our clinic during the past seven years in thirty-two cases in place of the Miles' operation as described above. The chief difference in the two operations is that in the Miles' operation the abdominal part of the operation is completed before the perineal part is undertaken, while with the modified technic the abdominal part of the operation is commenced but not completed until after the rectum has been removed through the perineal incision.

The object of using such technic is to facilitate dissection and to avoid soiling of the operative field in difficult cases. Patients selected have been those with very large bowels associated with much fat, extensive tumors and small pelves. Frequently, a combination of two or more of these factors were present. We have also employed it in a few cases of rectosigmoidal cancer when the disease had infiltrated the muscle coats and appearance suggested that the bowel might be ruptured by the usual traction and manipulation.

Operation is commenced in the usual manner for a Miles' dissection, incision, exploration and ligation of the inferior mesentery vessels. The decision as to technic is not determined until the pelvic findings are known. When the modified technic is to be employed, the lateral leaves of the mesocolon and mesorectum are divided and the incision carried across the midline anterior to the rectum. The rectum is separated from the sacrum. Further abdominal dissection will depend upon the individual case. In some instances abdominal dissection has been quite complete and in others rudimentary. After the abdominal dissection has been completed to the degree thought advisable, the sigmoid is divided. The distal segment is allowed to rest in the pelvis, and the proximal end of the bowel is brought through the original incision. Additional pads are placed in the wound to prevent any small bowel from entering the pelvis while the operation is in progress. These pads are held in position by the second assistant while the operation is continued.

The second part of the operation consists of dissection and removal of the bowel by the perineal route. The position of the patient is changed, the feet are placed in stirrups, the buttocks drawn down to the edge of the table, the perineal operative field draped, the anal canal closed and the perineal part of resection carried out in the usual manner. After the specimen is removed through the perineal incision, a hot pad is placed in the lower part of the pelvis,

and the perineal skin surfaces united by means of one or two sutures to hold the pad in place. Sterile towels are then placed over the perineal wound and the patient returned to his original position on the table. Gloves, gowns and drapes are changed and the operation is continued through the original abdominal incision. The new pelvic floor is constructed. The proximal end of the sigmoid is brought through the original or stab incision to form a colostomy. The abdominal wound is closed in layers and dressings are applied. The final step consists of removing the previously placed pelvic pad, inserting a glove pack into the hollow of the sacrum, closing the perineal wound with a few interrupted skin sutures and applying a perineal dressing. This technic might well be termed an abdominoperineal-abdominoperineal operation.

This modification of the Miles' operation may seem to be a clumsy and prolonged procedure due to changing of drapes, gloves, position of patient, etc. These changes do not require more than ten to fifteen minutes. This technic facilitates dissection and permits easy construction of the pelvic floor. This modification is not suggested for routine use but only in those cases in which the Miles' dissection cannot readily be accomplished, and in cases in which there is an increased possibility of soiling by rupture of the gut. In the thirty-three such cases in which this technic was employed, there were four postoperative deaths.

The third type of abdominoperineal resection, which has a limited field of usefulness but is worthy of consideration, is the two-stage Lahey[2] operation. This two-stage operation at one time enjoyed great popularity. It has its greatest field of usefulness when dealing with advanced operable disease in comparatively poor physical risks. In the last sixty abdominoperineal resections the two-stage technic has been employed in only two cases.

The most outstanding objections to abdominoperineal resections have been the high operative mortality and the permanent abdominal artificial opening. An abdominal colostomy, after a rectal resection in a clinically cured patient, is not a great handicap nor a very objectionable feature, provided the patient is taught how to care for the opening[3] and is fitted with a suitable abdominal support. The objectionable features of an artificial opening in a patient free of disease must not be confused with the objectionable features of a colostomy in a debilitated patient with incurable cancer. In the latter instance, many of the disagreeable features are due to the advanced disease and not to the artificial opening. A well functioning colostomy in a patient free of disease does not interfere with ordinary routine work or way of life. A large percentage of our patients, who are clinical cures, enjoy better health after operation, with a colostomy, than for many years before operation.

The operative mortality for abdominoperineal resections in recent years has shown marked improvement. In many private clinics it is now below 10 per cent, with a more favorable figure for small selected groups. In our clinic, at Memorial Hospital, which consists of both service and private cases, from January 1, 1931, to December 31, 1941, 128 cases were subjected to one-stage abdominoperineal resection with ten deaths, or an operative mortality of approximately 7.8 per cent. The last sixty-nine operations were completed without one postoperative fatality. Prior to 1942, an additional forty-four patients were operated upon by two-stage procedures. In this latter group there were five deaths or an operative mortality of 11.4 per cent. Operative mortality is influenced not only by surgical technic but also by postoperative and preoperative care of patients.

Preoperative preparation requires hospitalization of from five to fourteen days. Operation should be delayed until patients are relieved of intestinal stasis and the general physical condition has been raised to a status satisfactory for major surgery. The colon is cleansed by means of epsom

salt, sufficient to produce three to five stools daily, and by daily irrigations. During the past two years we have employed a high caloric low protein diet from the time of admission until thirty-six hours before operation. The day prior to operation cathartics are discontinued and diet consists of hard candy and fruit juices only. Liberal amounts of vitamins and intramuscular injections of liver are administered daily. Other factors necessary for improving the physical condition will be revealed by careful detailed physical and laboratory investigations. Laboratory investigations should include tests for liver damage, as a large number of patients with malignant disease of the terminal intestinal tract have been found to possess varying degrees of liver dysfunction.

The anesthetic in rectal resections is very important. We prefer spinal, using pantocaine and glucose, with liberal preoperative sedation. Spinal anesthesia may be supplemented with small amounts of pentothal sodium, when patients are restless and apprehensive. This technic has proved exceedingly gratifying during the past two years. While spinal is the anesthetic of choice, when properly administered and controlled, a general anesthetic is preferable to poor spinal.

All our patients receive a transfusion of bank blood during the operation, with additional infusions of glucose and saline as thought advisable. We have not used the sulfonamide group of drugs within the abdominal cavity as a means of preventing infection, nor have we employed them preoperatively. In a few of the recent cases, a small amount of sulfathiozole has been sprinkled in the pelvic wound before inserting the pack, as a means of decreasing the degree of infection and providing a cleaner wound when the pack is removed.

Postoperative care consists of maintaining the good physical condition obtained prior to operation, and relieving any surgical complications that may arise. Frequent blood chemical analyses are necessary to guide a satisfactory postoperative course for a number of these patients. In addition to the usual blood counts and hemoglobin estimation, one must include tests for liver damage such as prothrombin, serum protein, bilirubin, etc. When a satisfactory blood picture is maintained, the postoperative course is usually smooth and uneventful. Following operation, fluid balance is maintained by intravenous saline and glucose until such time as sufficient fluid can be taken by mouth. Low prothrombin levels may at times be raised by injections of vitamin K. Anemia and serum protein deficiencies are controlled by the administration of whole blood or blood plasma. During the past two years we have encountered a number of patients with liver damage whose condition was made worse by injection of whole blood but who were at once improved when blood plasma was administered. Surgical complications are not frequent but when they do occur require careful surgical judgment for diagnosis and treatment.

CONCLUSIONS

1. The Miles' one-stage abdominoperineal resection is the operation of choice for the majority of operable rectal and rectosigmoidal cancers.

2. The above described modification of the Miles' technic is considered an advantage in certain cases.

3. Patients with abdominal colostomies frequently enjoy better health than before operation.

4. The operative mortality in radical resections may be kept within a reasonable figure by careful surgical technic and by detailed consideration of the patient's condition prior to, during, and after operation.

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Case Reports

CHRONIC INTUSSUSCEPTION DUE TO SUBMUCOUS LIPOMA OF ASCENDING COLON*

CASE REPORT

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SUBMUCOUS lipoma of the colon is still apparently of sufficiently infrequent occurrence to warrant report when encountered clinically and, since resection of the bowel is a common method of treatment of this condition, such a report has the added advantage of providing the opportunity for discussion of some of the more important points appertaining to this surgical procedure.

The latest report to come to the notice of the writer is that of Gault and Kaplan[1] who also review the recent literature on the subject. These authors found reports of thirteen cases which had appeared since the publication in 1937 of the comprehensive article by Pemberton and MacCormack[2] and added one of their own. Pemberton and MacCormack reported a total of 116 cases of submucous lipoma of the large bowel, ninety-seven of these having been clinical cases which manifested symptoms, while in the remaining nineteen the condition was discovered only at autopsy. The fourteen additional cases in Gault and Kaplan's report all belong to the clinical group.

Those lipomas which qualify for admission to this group possess the intriguing interest of always being able to foil the diagnostic efforts of the clinician, for the symptomatology to which they give rise is not specific in character for lipomas, as such, but is simply that of the complications which may result from the presence of any tumor of the bowel. Even at operation inspection of that part of the bowel in which the tumor is situated and palpation of the tumor itself through the wall often leave the diagnosis in doubt, the true nature of the tumor not being revealed until either the bowel is opened or the resected specimen examined.

In brief, the symptoms are those of intestinal obstruction with or without melena. The former are consequent upon either the growth of the tumor to a size sufficient to encroach upon the lumen of the bowel to such an extent as to interfere with the onward passage of the fecal contents or due to its presence stimulating the musculature of the bowel sufficiently to attempt its extrusion by forcible contractions, with the production of an intussusception. The obstructive symptoms vary in intensity and are usually of a mild, chronic type but on occasions more severe symptoms, in the form of definite acute attacks, render more urgent the patient's desire for medical advice. Acute symptoms, however, are not nearly so likely to be present as when these tumors are situated in the small bowel. Melena, should it occur, is usually due to erosion of the dome of the lipoma or, more rarely, to pressure ulceration of the adjacent mucous membrane, as in the case

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about to be reported, and commonly takes the form of repeated, small hemorrhages.

Pemberton and MacCormack mention that a palpable abdominal mass was present in sixty-four of the ninety-seven clinical cases they reported, indicating this finding to occur on the average in two out of every three cases. In Gault and Kaplan's fourteen cases much the same average was maintained, for a tumor was palpable in eight. While the presence of such a mass may be due to the tumor itself, an intussusception associated with the tumor or the accumulation of fecal matter just proximal to it may be the factor determining whether or not a mass will be palpable. The case about to be reported is of particular interest in connection with this physical sign.

For the nearest approach to the correct diagnosis we usually have to rely upon the barium enema but, as with the symptomatology, a lipoma gives no characteristic findings. However, in the presence of a lipoma giving rise to symptoms, this roentgenological procedure rarely fails to disclose evidence of pathological change in the large bowel, even though the information may be given to us in such general terms as "filling defect," "polypoid tumor," "obstructive lesion" or "intussusception" or, more specifically, and wrongly, as "carcinoma." Nevertheless, the knowledge obtained from the administration of a barium enema is thus of the greatest importance for it will not only tell us definitely of the presence of a pathological lesion of the large bowel but will also often localize it for us and so provide the necessary information upon which operation can be justifiably advised and intelligently planned.

It is generally agreed that the frequently long clinical history associated with a lipoma, the usual good general condition of the patient and the absence of weight loss are features which tend to deny the common roentgenological diagnosis of carcinoma. However, these features point only to the probability of a benign lesion being the cause of symptoms, but such a lesion is much more likely to be an adenoma rather than a lipoma. In a series of autopsy specimens of polypi of the intestine reviewed by the writer[3] some years ago, only two out of forty-four of those in the colon were lipomas, while no less than thirty-six were of the adenomatous type.

The treatment of a submucous lipoma of the colon consists essentially of surgical removal and, while in some cases this has been done by incising the bowel and removing the tumor, the more usual procedure employed has been a resection of the tumor-bearing segment of the bowel in one or more stages.

CASE REPORT

Mr. R. F. was admitted to the Santa Barbara Cottage Hospital on March 26, 1940, his complaint being hemorrhage from the rectum. The day before admission he had passed "about a pint" of blood per rectum in the form of clots, both black and red in color, following a movement of the bowels. This was the only severe hemorrhage he had ever experienced.

For the past three years he had suffered from chronic constipation, having nearly always to resort to the use of an enema in order to obtain a bowel movement. During this time there had been no attacks of diarrhea but on occasions he had passed small amounts of blood. From time to time he would be seized with lower abdominal pain which was never colicky but always of a dull, aching character. He noticed that an evacuation of the bowels would always relieve the pain but on several occasions, when he had not been able to obtain relief in such a manner, a lump would develop in the left side of the abdomen, to disappear when the bowels eventually moved. He had often been troubled with tenesmus and his stools appeared to him to be no greater than a pencil in diameter.

His appetite was good and he had no indigestion. During the past year he had noted a loss in weight of a few pounds.

The patient was a well nourished man who appeared in good health. His systolic blood pressure was 118 mm. of mercury and his diastolic, 80. Heart and lungs were normal. The abdomen was soft, there were no tender areas and careful palpation failed to reveal the presence of a mass. (Abdominal examination was repeated daily before operation but always

with this same result.) Rectal examination revealed nothing of importance. Urinalysis was negative and the blood showed a hemoglobin of

FIG. 1. Film of preoperative barium enema showing marked dilatation of transverse colon and incomplete filling of cecal area.

13.5 Gm. (90 per cent), 4,510,000 red cells and 7,050 white cells with a normal differential count. Examination of the feces was positive for blood by the Benzidene test and no parasites or ova were found.

A barium enema was administered and the following report was given by Dr. Milton Geyman:

The distal colon filled without evidence of filling defect as observed during screen study. The transverse colon, and more particularly the hepatic flexure, was markedly widened. At the cecum the barium column met a mass which prevented filling of this region. The enema pressure was continued for several minutes without further filling. Gentle palpation was also unsuccessful. No mass could be palpated over this area of incomplete filling.

A film study made before evacuation shows the above picture. (Fig. 1.) A film after this had taken place shows almost complete emptying of the colon. An abnormal mucosal pattern is shown in the splenic flexure area. The proximal colon is completely empty except for a tubular segment of rather peculiar arrangement. There is no evidence of obstruction proximal to the cecum in the way of gaseous meteroism.

The incomplete filling of the cecal area suggests an intussusception even though no mass is palpable. The arrangement of the barium coating, as shown in the after-evacuation film, in the splenic flexure suggests a diffuse marginal infiltration, probably on a carcinomatous basis.

Operation was performed on April 2, 1940, under a general anaesthetic of nitrous oxide, oxygen and ether. The peritoneal cavity was opened through a right paramedian incision, the rectus muscle being retracted laterally. A portion of the transverse colon presented and this was seen to be of normal color, but markedly dilated and on palpation it was abnormally bulky. On passing the hand distally along the colon a mass about the size of a large tangerine and of firm consistency was discovered a few inches proximal to the splenic flexure. Examination of the proximal portion of the colon revealed that the cecum, most of the ascending colon and several inches of the terminal ileum were invaginated into the transverse portion of the large bowel. The reduction of this intussusception was accomplished without difficulty and, when completed, the tumor previously felt near the splenic flexure assumed its rightful place in the ascending colon about three inches above the ileocecal valve. Its surface was slightly nodular and it was thought to be a large adenomatous polyp although the possibility of polypoid carcinoma was considered. However, there were no enlarged glands along the course of the right colic artery and the liver was free from metastatic deposits. The ileum was not dilated nor did its terminal portion, which had been part of the intussusceptum, show any abnormal change.

It was decided to do a formal resection of the terminal few inches of the ileum and the right half of the colon. This was carried out, the cut ends of the ileum and the transverse colon being closed by inversion and the continuity of the bowel re-established by an isoperistaltic side-to-side anastomosis. The abdominal wound was than closed in layers without drainage.

Pathological Report. (*Dr. Clark Brown.*) Gross: The specimen consists of a segment of terminal ileum, cecum and proximal colon. (Fig. 2.) The large intestine measures 22.0 cm. from the ileocecal valve to the point of excision. A strip of mesenteric fat is attached to the specimen. Nine cm. above the ileocecal valve a polypoid structure measuring 7.0 by 4.0 by 4.0 cm. extends into the bowel lumen. This is covered with intact mucosa on all surfaces.

Section shows it to be composed of firm, glistening fat. The tumor is attached to the bowel wall by a short pedicle 1.0 cm. long and 2.0 by 1.0 cm. on cross section. Beside the pedicle is an area of irregular superficial ulceration measuring 2.0 by 2.0 cm. It appears to have resulted from frictional contact with the polyp. The remainder of the mucosal surface of the large bowel appears normal. An appendix 9.0 cm. long and 0.7 cm. in diameter is attached to the cecum. The surface is smooth, the wall of usual thickness and the lumen contains fecal material.

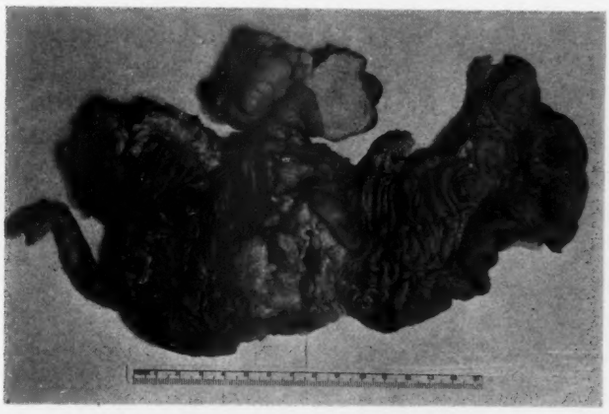

FIG. 2. Photograph of resected specimen with tumor bisected to show its lipomatous character.

Microscopic. Section of the polyp shows it to be composed of a core consisting mostly of mature fat cells. Strands of fibrous tissue, a nodule of smooth muscle and scattered foci of lymphocytes are also seen in the polyp. It is covered with mucosa. In the section of adjacent colon the mucosa is seen to be ulcerated. The submucosa contains lymphocytes, fibroblasts and macrophages. Mesenteric lymph-nodes included with the specimen are hyperplastic and edematous.

Diagnosis. Lipomatous polyp of the colon with contact ulceration.

The postoperative course was uneventful. The wound healed per primam and the patient left the hospital seventeen days after his operation. He returned for examination a month after leaving the hospital and by that time was already doing light work at his job as a carpenter. The abdominal wound was firm and, in marked contrast to the constipated state of his bowels for the three years previous to his operation, he was having regular daily bowel movements.

He was seen again in September, 1941, eighteen months after his operation. He reported that he was in excellent health, that he had never lost a day's work except through an attack of "flu" and that he had continued to have a bowel movement daily. At this time he was given a barium enema, a photograph of the film of which is shown in Figure 3. The following is the report on this enema: The colon was studied by a barium enema administered under fluoroscopic control. The mixture passed without difficulty all the way through the colon. The cecum, ascending colon and hepatic flexure have been resected and now there is what appears to be a side-to-side anastomosis between the terminal ileum and transverse colon at a point approximately two inches from the stump of the resected colon. There is no evidence of infiltration, obstruction or other abnormality at the site of the anastomosis and no abnormality is demonstrated in the colon or terminal ileum.

COMMENTARY

This was yet another case of lipoma of the colon in which the roentgen diagnosis was that of a lesion of probable carcinomatous nature while the clinical features of a long history, a general condition of the patient lacking any suggestion of cachexia and the mild degree of weight loss pointed to the presence of a benign lesion. However, there were two features present in this case which are not commonly mentioned in other case reports and are therefore of interest. The first was the occasional appearance of a mass felt by the patient in

the left side of the abdomen. Its disappearance always and only after a bowel movement had taken place seems to indicate

Fig. 3. Film of barium enema eighteen months after operation. The remaining colon is of normal caliber and the stoma between ileum and colon is functioning well.

that it was due to an accumulation of feces behind the tumor, for while the patient was under observation for several days prior to the operation, during which time a daily enema was given with satisfactory results, repeated careful abdominal examination failed to elicit the presence of a mass. However much the increased bulk of the transverse colon due to the intussusception might have added to the size of the tumor, it was insufficient to do so to the extent of rendering it palpable; for the bowel was found intussuscepted at operation and no mass was palpable immediately before the abdomen was opened. The second unusual feature was the type of hemorrhage and its origin, the former because in these cases severe hemorrhage is the exception to the general rule of repeated small ones, although these had taken place; hitherto, the only source of hemorrhage reported in a case of lipoma appears to have been an erosion of the dome of the tumor, but in this case such a superficial ulceration occurred, not on the tumor itself, but in the mucous membrane of the bowel close to the short pedicle and it was apparently from this ulcer that the hemorrhage had originated. Ulceration in this situation is of further interest in that it supports the thesis that the intussusception was caused, not by the passive drag of the tumor on the bowel wall, but by the active efforts of the bowel musculature to extrude what was virtually a foreign body. In endeavoring to do so the bowel wall contracts down upon the tumor and this abnormally contracted part is forced by increased peristaltic movements through the abnormally relaxed portion of the bowel below. The repeated contraction of the bowel wall down upon the tumor is a reasonable explanation of the occurrence of ulceration of the bowel mucosa through pressure of the tumor upon it.

A tumor having been found inside the ascending colon, the question then arose as to the best procedure which should be adopted to accomplish its removal, the answer to which question depended largely upon the probable pathological condition present. It was sufficiently hard in consistency to have been a frank polypoid carcinoma although, since the tumor was of such a large size, the absence of enlarged glands in particular weighed rather heavily against this diagnosis. As a benign tumor, its most likely pathological status was that of an adenoma for, as mentioned previously, this is by far the most common type of benign tumor of the large bowel. It was demonstrated clearly by the writer in his review, to which reference has already been made, not only that adenomas are capable of undergoing malignant change but that this may be expected in any adenoma which has grown to about the size of a walnut. Since this tumor greatly exceeded such proportions, it could be taken for granted that malignant change was present if the probable diagnosis of adenoma were correct. These considerations, in conjunction with the good general condition of the patient, were those responsible for the

decision to perform a resection of the proximal half of the colon as the method of choice of removal of the tumor, since a local extirpation through an opening in the bowel can never be accepted as an adequate form of treatment for a large adenoma owing to the danger of leaving behind imperceptible malignancy in the bowel wall. The true nature of the tumor was thus not determined until the resected specimen was examined.

Of particular interest to the writer are the cases in which the resection of this portion of the colon has been undertaken in multiple stages and especially those which have included, not the closed ileocolostomy, but the open type, thus necessitating a period of several weeks during which the patient must submit to the nuisance (to say the least) of an abdominal anus and prolonging into months the time that he must be under surgical care. As the outcome of his personal experience, the writer has come to the conclusion that, in cases in which resection of the right half of the colon is indicated as the treatment of choice, whether this be for the presence of benign tumor, hyperplastic tuberculosis or malignant disease, to mention the three conditions for which this operation is most commonly performed, the need for any procedure other than the single-stage operation rarely arises. Only in the minority of cases, such as those in which obstruction has resulted in changes in the bowel or in which the general condition of the patient leaves much to be desired, need it be considered advisable or necessary to complete the resection in more than one stage. When for such reasons it is decided to do the operation in multiple stages, the writer believes that a primary ileocolostomy, to be followed by the secondary resection, is the procedure of choice. However, the Mikulicz type of operation still appears to have considerable popularity[2] although it is difficult to see what advantages it possesses over the two-stage method just mentioned. In the first place, the first stage of the Mikulicz operation entails a mobilization of the bowel just as extensive as when primary resection is performed. Furthermore, it would seem that if the patient can withstand the dissection necessary for this mobilization, he can certainly also withstand the additional resection which, on completion of the mobilization, takes but little time and should in no way jeopardize his chances of recovery from the operation. Once the resection has been done, there remain the basic alternatives of either exteriorizing both cut ends of the bowel in the form of a double-barrelled colostomy or at once restoring the continuity of the bowel by an anastomosis. The disadvantages inherent in the former have been mentioned briefly and, from the patient's standpoint, they should be sufficient to deter the surgeon from performing this procedure whenever possible. The chief argument used against the latter alternative is the risk of leakage of intestinal contents at the site of anastomosis, leading to a peritonitis which, should it happen to occur, is generally fatal.

It is, therefore, important to examine the etiological aspect of anastomotic leakage. In cases in which this catastrophe has occurred it is interesting to note that the anastomosis has almost invariably included an "end," that is, it was of the end-to-end or end-to-side type. Moreover, in reports of such cases it usually appears to be inferred that the blame for leakage has primarily to do with the actual line of suture rather than with the bowel itself. The fact is, however, that the success or failure of such an anastomosis is largely determined before the first suture has even been begun. The reason for this is that the essential factor responsible for the success of any "end" anastomosis is the conservation of the blood supply of the bowel right up to its cut edge. Failure to carry out this conservation, whether unwittingly or through lack of appreciation of its fundamental importance, is likely to end in disaster no matter how carefully, or by what technic, the anastomosis is performed, for one or

more areas of necrosis will occur immediately adjacent to the cut edge of the bowel and, should the extent of any one of these areas reach beyond the completed line of suture, it will provide a path of escape for intestinal contents into the peritoneal cavity. Clinical support of this thesis is to be found in the postoperative histories of cases in which leakage occurred, for the symptoms of peritonitis do not usually appear within the first twenty-four hours, as they would if the suturing had been faulty (surgeons experienced enough to be performing bowel resections are not likely to be guilty of failure to make a water-tight anastomosis) but have their onset after a latent period averaging from four to six days, this period representing the time it takes for necrosis to occur.

If this conservation of the blood supply is borne in mind, then in most cases it can be achieved with ordinary care, but it is possible for the most painstaking surgeon to make an error in judgment regarding the site of division of the mesenteric or mesocolic vessels necessary to ensure it. A great help in preventing failure to conserve the blood supply lies in relaxation of the clamps, following which the amount of hemorrhage from the cut edge of the bowel can be observed; should bleeding be absent or scanty, enough of the end of the bowel can be removed until the desired brisk hemorrhage is seen to take place. (A distinct disadvantage of the "aseptic" technic in an "end" type of anastomosis is that it prohibits this relaxation and so denies to the surgeon the certainty that he has conserved the vascular supply to the cut edge of the bowel, on which condition the success of the anastomosis primarily depends.) An even safer procedure to adopt, however, when enough bowel is available, is one which will make due allowance for the possibility of failure to conserve the blood supply having occurred in spite of whatever precautions might have been taken to avoid this outcome. This procedure consists simply of closing the cut end of the bowel by inversion, the rationale of doing so being that any area which might have become necrotic and so allow leakage will be safely tucked inside the inverting sutures.

When a side-to-side anastomosis is performed, an adequate blood supply to the edges of the bowel incision is assured and here any leakage can thus be attributed directly to a faulty anastomosis and, therefore, should not occur. The small amount of soiling of the peritoneum which is all that is permitted by ordinary careful technic when doing a bowel anastomosis is not sufficient to cause a general peritonitis.

These considerations have led the writer to hold the opinion that, in single-stage resection of the right half of the colon, the danger of leakage from the anastomosis can be averted by inversion of the cut ends of the bowel and the re-establishment of its continuity by side-to-side anastomosis. Up to the present this procedure, which represents the practical application of these considerations, has never failed to achieve its object whenever it has been employed by him, for no instance of leakage has occurred. When this particular resection is done, there is always enough bowel available to permit of this type of anastomosis being performed without undue tension.

The advantages accruing from the single-stage resection of the proximal part of the colon, with inversion of the cut ends of the bowel and side-to-side anastomosis are well exemplified by the present case. The patient had the uneventful recovery the writer has come to expect in cases following this operation and was in the hospital no longer than he would have been for any other major, and perhaps less severe, abdominal procedure. This is in marked contrast to the burden, both economic and surgical, which he would have had to bear had the Mikulicz type of operation been performed.

SUMMARY

1. A case is reported of chronic intussusception due to a submucous lipoma of the ascending colon.

2. The roentgenological diagnosis was probable carcinoma of the splenic flexure.

3. Two unusual features were present: (a) The symptom which caused the patient to seek medical aid was a severe hemorrhage from the rectum. (b) The apparent source of the hemorrhage was an ulceration of the mucous membrane of the bowel situated close to the short pedicle of the tumor.

4. A single-stage resection of the terminal few inches of ileum and proximal half of the colon was performed, the ends of the ileum and colon being inverted and the continuity of the bowel re-established by a side-to-side anastomosis. It is considered that in cases in which resection of this portion of the bowel is indicated as the treatment of choice, the need for any procedure other than this single-stage operation rarely arises.

5. The etiology of anastomotic leakage is discussed and it is emphasized that the essential factor upon which depends the success of any "end" anastomosis is the conservation of the blood supply of the bowel right up to its cut edge. The success which attends the type of anastomosis referred to above lies in the fact that it is both an easy and safe method of guarding against a failure to conserve this blood supply, when such failure might readily result in leakage if an "end" type of anastomosis were performed.

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COLLOID ADENOCARCINOMA OF THE URACHUS*

REPORT OF TWO CASES

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IN the clinical evaluation of tumors of the bladder a distinction should be made between the more commonly seen papillary and solid tumors and the rare adenocarcinomas found in the vault of the bladder. These adenocarcinomas arise from the epithelium of the urachal canal and are in reality not tumors of the bladder at all, but merely masquerade as such after they have invaded the bladder mucous membrane.

The work of Begg (1930)[1] added to the knowledge concerning the anatomy, histology and development of the urachus. According to Begg, the urachus developmentally is the upper portion of the anlage of the bladder and is derived from the ventral cloaca. In the adult it is a cone-shaped structure approximately 5 cm. in length extending from the bladder to the umbilicus. The urachus is lined by an irregular form of transitional epithelium.

Begg (1931)[2] collected forty-four cases of tumor of the urachus from the literature. These were classified as follows: Fibroadenoma—3; adenocarcinoma—4; colloid adenocarcinoma—19; mixed tumor—8; fibroma and fibromyoma—4; sarcoma—6. He states that the colloid adenocarcinoma represents primarily a metaplasia of the transitional epithelium followed by a colloid or mucoid degeneration. Sections appear very much like rectal carcinoma.

Kalo (1931),[3] Payne and Jones (1931),[4] Ferrier, Craig, and Foord (1936),[5] Begg (1936),[6] De Waard (1939),[7] Mattel (1940),[8] and others have added cases of adenocarcinoma of the urachus to Begg's original list.

We wish to present the following two cases of colloid adenocarcinoma of the urachus:

CASE REPORTS

CASE 1. The patient, a white, married male, physician, aged fifty, was admitted to the Urologic Service at the Hospital of the University of Pennsylvania on August 26, 1940, with the complaint of gross hematuria of six hours' duration.

The patient was well until the day of admission when while voiding he had the sensation that all of the liquid coming from his bladder was not urine. On observing the stream he found bright red blood. There was no pain at the time. The hematuria persisted each time he voided. When he was admitted about eight hours later he was passing clots which caused him discomfort. There was no history of previous hematuria, frequency, nocturia, urgency, pyuria, or other urinary symptoms.

A weight loss of seven pounds had occurred in the past year. He was operated upon for a ruptured appendix in 1936. His family history revealed no points of clinical significance.

Physical examination showed a well developed and nourished white male, aged fifty, not acutely ill. The chest was clear. The heart was not enlarged, the blood pressure was 130/80. There were no murmurs. In the right lower quadrant of the abdomen there was an old operative scar. The external genitalia and rectum revealed no significant findings.

Laboratory examinations showed the following findings: red cell count 4,780,000, white cell count 7700, blood urea nitrogen 6 mg. per cent, blood sugar 82 mg. per cent. The urine was alkaline and free of sugar, but albumin, red cells, and white cells were present.

Under larocaine anesthesia a No. 24 cystoscope was passed with ease to the bladder. The entire bladder cavity, ureteral orifices and

* From the Urologic Service of the Hospital of the University of Pennsylvania.

vesical neck appeared normal except for a small opening in the fundus which appeared to be about 2 cm. in diameter. Through this hole was projecting a cluster of tiny fronds which appeared very friable.

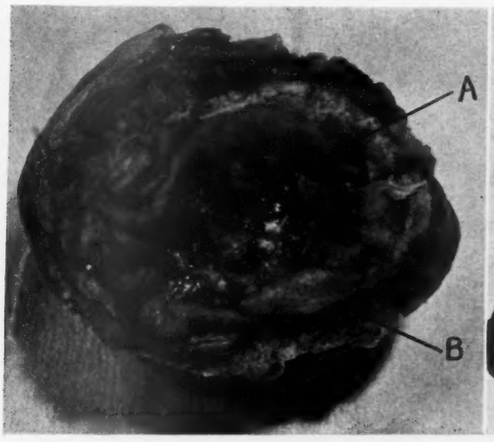

Fig. 1. Gross specimen of resected tumor from Case 1. The surface presenting itself to the bladder is shown. A, the ulcerated surface of the neoplasm; B, the bladder wall consisting of mucosa, muscle and serosa.

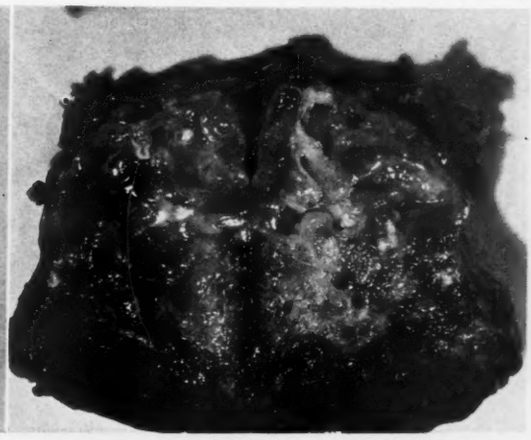

Fig. 2. Gross specimen of resected tumor from Case 1. A longitudinal section through the mass is shown. Observe the mucoid appearance of the tissue.

The bladder was examined by means of opaque solution and air. The only unusual finding was along the upper border of the bladder where there was a serrated appearance. This same finding was also present on the pneumocystogram.

Through a midline incision from the pubis to the umbilicus the muscles were divided and the peritoneum exposed. A firm conical shaped mass was palpated and found to be projecting above the uppermost portion of the bladder. The peritoneal cavity was opened and the omentum was found to be adherent to the growth at one point. The omentum was doubly clamped above the attachment to the tumor mass, divided between the clamps and the proximal portion ligated. The peritoneum was incised on either side of its bladder reflection and this incision was carried well below the tumor mass. The peritoneum was then further dissected from the lower posterior portion of the bladder wall. This procedure completely freed the upper half of the bladder with the tumor mass. The peritoneum was then closed beneath the bladder with a suture of plain No. 1 catgut.

The bladder was now opened and the previously instilled mercurophen solution aspirated. The upper half of the bladder, containing the growth, was now removed. A collar of approximately 1.5 cm. of healthy bladder was taken with the tumor. The bladder was then closed with interrupted sutures around a large Pezzer catheter. The skin, subcutaneous tissue and muscle were closed with figure-of-eight sutures of silkwormgut. A skin clip was placed at either end of the incision.

The suprapubic tube was removed on the tenth postoperative day. The fistula closed on the fifteenth postoperative day. The patient was discharged on the twenty-first postoperative day.

The specimen consisted of a tumor removed from the region of the urachus. It measured 6 by 4 by 4 cm. and appeared to be encapsulated. On section it was pale, mucoid and showed deposits of calcium. Microscopic diagnosis: Adenocarcinoma of the urachus with colloid degeneration.

The patient is alive and well at this time. There are no evidences of recurrence or metastases.

Case II. The patient, a white male, aged forty-nine, was admitted to the Urology Service at the Hospital of the University of Pennsylvania on February 27, 1942, with the complaints of frequency of urination and hematuria.

He was in good health until three years ago. At that time he observed that he had to empty his bladder more frequently than normal both during the day and at night. There was also burning on urination. These symptoms persisted and three months ago he first observed

blood in the urine. He received irrigations of the bladder and symptomatic treatment from his local physician. However, the bleeding

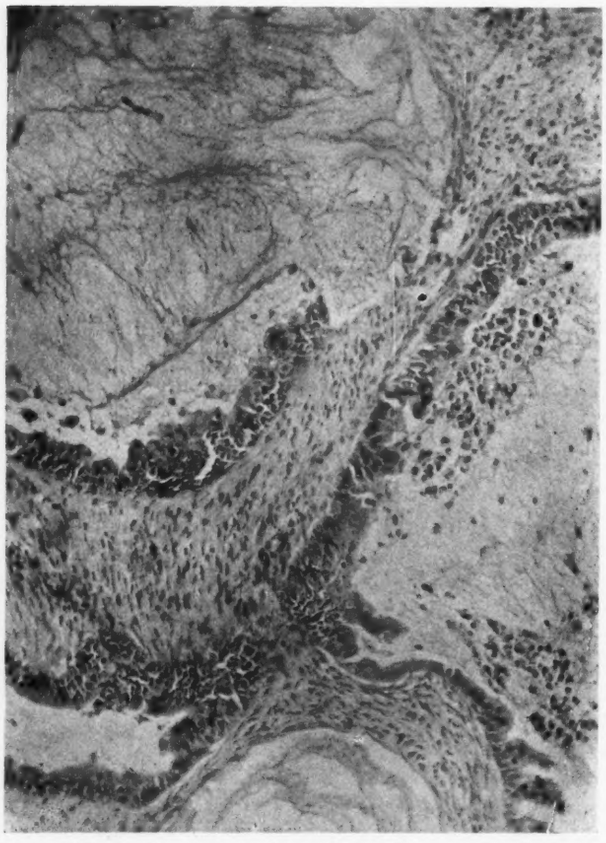

FIG. 3. Photomicrograph of a section of the resected tumor from Case 1. Observe the typical appearance of a colloid adenocarcinoma of the urachus.

became worse so he finally decided to come to the hospital. Thirty-five pounds of weight had been lost in the past year.

Physical examination showed a pale, white male, aged forty-nine, who appeared to be chronically ill. The chest was clear and the heart was not enlarged. The blood pressure was 130/60. There was a harsh systolic murmur at the apex. The abdomen was free of any palpable masses. The external genitalia showed no abnormality. Rectal examination showed a small, smooth, firm movable and symmetrical prostate.

Laboratory examinations showed the following findings: hemoglobin 34 per cent, white cell count 10,000, blood urea nitrogen 13 mg. per cent, and phthalein excretion of 75 per cent in two hours. The urine was alkaline and contained albumin and many red blood cells and white blood cells. Urine culture showed Streptococcus viridans and Staphylococcus albus, but no tubercle bacilli.

The chest was clear. Intravenous urogram showed excellent dye excretion on both sides. "There was some dilatation of both ureters in their juxta-vesicular portion. The bladder was quite small and trabeculated. These findings suggest inflammatory changes in the adnexa and probably in the bladder itself." Cystoscopy: The entire bladder dome to a point just above the trigone was extensively involved as a fungating necrotic mass.

The patient was given three blood transfusions of 500 cc. each. The hemoglobin reached 63 per cent. Bleeding from the bladder continued and in spite of transfusion he appeared to be getting weaker.

A midline incision was made from the pubis to a point two-thirds the distance between the pubis and the umbilicus. The muscles were retracted. An attempt was made to strip the peritoneum from the anterior and superior surface of the bladder, but it was densely adherent and involved with neoplastic tissue. The tumor mass extended to the height of the umbilicus and laterally it was firmly attached to the structures of the bony pelvis. A stab wound was made into the bladder on its anterior surface in the midline and the previously instilled antiseptic fluid aspirated. The incision was enlarged superiorly allowing visualization of the bladder contents. The entire bladder with the exception of the trigone, vesical neck, and ureteral orifices was involved with hard neoplastic tissue. A suprapubic tube was placed in the bladder. A portion of the neoplasm was taken for examination. The bladder was closed with interrupted sutures of plain No. 1 catgut. The muscles, fascia and skin were closed with vertical figure-of-eight sutures of silkworm gut.

The patient's convalescence was uneventful. He was discharged on April 1, 1942, with the suprapubic tube in place.

Pathologist's Report: The biopsy of the bladder lesion showed on microscopic examination masses of colloid material with a few scattered pyknotic cells in acinus-like arrangement. Diagnosis: Colloid adenocarcinoma of the urachus.

DISCUSSION

The age incidence of urachal carcinoma is the same as found in all epithelial tumors

the great majority being in the fifth decade and above. About 80 per cent of the reported cases are in males. Once the urachal carcinoma has invaded the bladder mucosa and penetrated the bladder, the clinical history and symptoms resemble those in ordinary tumors of the bladder. Appearance in the urine, however, of jelly-like masses is pathognomonic of a penetrating urachal adenocarcinoma. Before the urachal carcinoma invades the bladder mucous membrane, there are no urinary symptoms. Frequently, a mass can be felt suprapubically. In some cases cystoscopically an indentation of the mucous membrane can be seen at the apex of the bladder as a prelude to actual invasion. When the tumor penetrates the bladder, the cystoscopic picture is by no means uniform. The appearance may simulate papillary carcinoma or necrotic ulceration. There may be only a small opening at the apex of the bladder from which a gelatinous substance oozes. Furthermore, the point of bladder invasion may be eccentric in location due to the tumor extending laterally in the bladder wall before penetrating the mucosa. When the bladder penetration is extensive, typical long gelatinous fronds can be seen cystoscopically and, as previously mentioned, these frequently are extruded in the urine.

There is one uniform negative characteristic, urachal tumors are never pedunculated. Distant metastases are rare and occur late. Direct extension into the abdomen frequently occurs. The usual finding has been complete encapsulation of the supravesical portion of the tumor. In our second case this was not so. In the bladder wall the tumor invades the muscular coat without any semblance of encapsulation. This, of course, means that a generous portion of the bladder wall should be resected with the tumor.

The differential diagnosis is most important. Urachal carcinomas must be distinguished from urachal cysts, urachal abscess and tumors of the female adnexa. It is important that urachal colloid carcinomas be differentiated from the usual epithelial tumors of the bladder. The urachal tumors are primarily supravesical and are, therefore, not amenable to any endovesical methods of treatment. Complete surgical removal is the only means of effecting a cure.

Case I which was seen six hours after the onset of hematuria was amenable to surgical excision and after almost two years appears to evidence a complete clinical cure. In Case II, however, the hematuria had been of three months' duration and the cystitic symptoms of three years' duration. Extension of the tumor precluded complete surgical removal so only a palliative procedure could be done.

SUMMARY

Two cases of colloid adenocarcinoma of the urachus are described. The diagnosis and treatment of this condition are discussed.

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MASSIVE MIXED TUMOR OF THE SUBMAXILLARY GLAND*

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TUMORS of the submaxillary gland are far less common than are growths developing in the parotid. The present case of submaxillary gland tumor is reported because of the interest it created regarding both diagnosis and management. The literature contains numerous reports of parotid tumors and it is not surprising that much less attention has been devoted to the more uncommon submaxillary growths.

According to Ewing[1] three groups of epithelial tumors occur in the salivary glands: These are the true adenomas which are rare, the relatively more frequently found carcinomas and the mixed tumors.

The origin of the mixed tumors has long been a subject of active controversy. The histological structure of these neoplasms is complex, the epithelial elements usually taking the form of cell strands, alveoli or diffuse masses. The mesoblastic portion of such neoplasms consists chiefly of fine connective and mucous tissue and in many instances cartilage is present. It is of interest that the tumors are not always in obvious connection with the gland. Such tumors may be found in the floor of the mouth, in the retropharyngeal tissues or in any part of the lateral wall of the neck.

One of the most complete studies of mixed tumors of the salivary glands is that of McFarland.[2,3] After carefully studying a collection of 300 cases in which attention was given to history, operative findings, microscopic study and a follow-up over a period of years, a number of rather striking conclusions were reached. McFarland believed that the microscope offered little or no aid in determining the likelihood of recurrence of mixed salivary gland tumors.

Recurrences were found to occur any time from immediately after the operation up to forty-seven years later. While little definite help regarding recurrences of the mixed tumors was given by the microscope, he definitely believed that tumors removed while they were still quite small were far more likely to recur. This was credited to the greater likelihood of overlooking a small bit of tumor tissue. It was also reported that radium and *x*-ray offered no advantage over surgery in the treatment of such cases.

CASE REPORT

J. P., a colored male, age fifty-eight, was referred to me July 30, 1941, by Dr. J. T. Davis of Corinth, Mississippi. The patient complained of a large tumor on the left side of the neck which was first noticed twenty-five years before. At the onset the tumor presented as a small mass below the body of the mandible. The growth gradually became larger and prior to admission caused the patient considerable inconvenience, chiefly because of its size. Four months before admission the floor of the mouth was found to be elevated on the left side. Examination revealed a mass that extended from the body of the mandible to a point about 1½ cm. above the clavicle. Posteriorly the mass lay beneath the sternocleidomastoid muscle and anteriorly it extended almost to the midline. The floor of the mouth was elevated on the left side. The tumor could be moved slightly from side to side but could not be moved in the vertical direction. The greater portion of the mass felt solid, however, an area 4 by 4 cm. near the apex of the tumor was cystic on palpation. The other general findings were normal.

At operation, novocaine anesthesia was used, the cervical nerves being blocked near the transverse processes of the cervical vertebrae on the left side. Some additional infiltration was carried out along the posterior border of

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† Dr. Wilson is now on active duty as a Major in the Medical Corps, A.U.S.

the sternocleidomastoid muscle. An incision through skin and fascia was made along the anterior border of this muscle. The tumor was

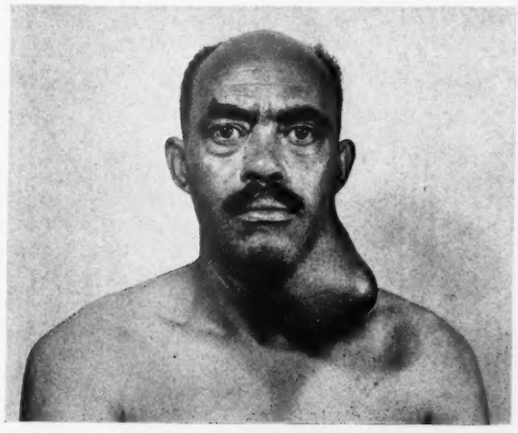

Fig. 1. Mixed tumor of left submaxillary gland of twenty-five years' duration.

well encapsulated and contained no true pedicle. It was in intimate contact with the carotid sheath from which it was dissected free. The wound was closed with interrupted sutures and healed within a week. Follow-up examination six months later showed the patient to be apparently entirely well.

The gross pathological specimen consisted of a mass of tissue 13 by 9 cm. At one pole of the tumor was a cystic area 3 cm. in diameter. The tumor had a thick fibrous capsule. On section it was seen to consist of firm, whitish tissue which was divided into lobules by fine strands of connective tissue. The cystic portion of the tumor was filled with brownish fluid. This probably represented an area of degeneration.

Microscopically, the tumor, which was well encapsulated, was made up largely of epithelial cells. These cells were arranged in cords and sheets and in some areas tended to form alveoli. The cells had nuclei which were oval or polyhedral in shape. The cytoplasm was granular and the cytoplasmic edges were rather indistinct. Scattered throughout the tumor were areas of fine fibrillar connective tissue shown exceptionally well by the Mallory stain. This fine connective tissue enmeshed mucus which was best demonstrated by the mucocarmine stain. No areas of true cartilage were seen.

COMMENT

Because of the long history and lack of fixation of the tumor it was believed that the lesion was benign. The referring physician strongly considered the diagnosis of carotid body tumor because of the location

Fig. 2. Gross specimen of benign mixed tumor of submaxillary gland.

of the mass and because lateral movement was possible while vertical movement was not. The author was of the opinion that a tumor arising from branchial cleft remnants should be strongly considered as well as that of a tumor of the submaxillary gland. A definite diagnosis was reached only after a careful microscopic study of the tumor.

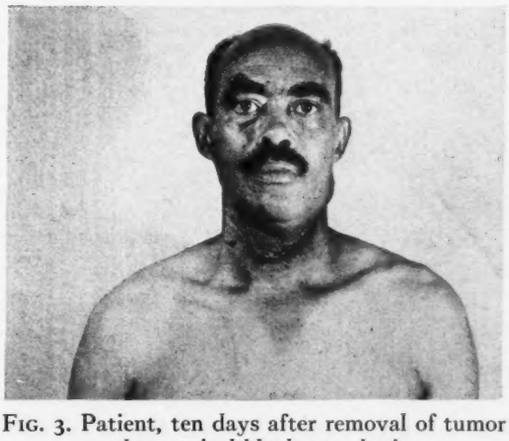

Fig. 3. Patient, ten days after removal of tumor under cervical block anesthesia.

Regional anesthesia as given by cervical block was considered the anesthetic of choice since it caused the patient relatively little general disturbance and also made it possible for the patient to co-operate throughout the operation. Such co-operation is of aid in preserving the facial nerve which is not infrequently distorted by such growths.

SUMMARY AND CONCLUSIONS

1. Three types of epithelial growths occur in the salivary glands, these being in the order of their occurrence the mixed tumors, carcinomas and the relatively rare true adenomas.

2. Mixed tumors of the submaxillary gland clinically and histologically resemble those of the parotid although the latter tumors are encountered much more frequently.

3. Salivary gland tumors do not always arise in the conventional location as they may occur in the floor of the mouth, in the retropharyngeal region or in the lateral walls of the neck.

4. A case of a massive mixed tumor of the submaxillary gland successfully removed under local anesthesia is reported.

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Nitrous oxide and oxygen may be administered simultaneously to supplement spinal anesthesia when blood pressure is satisfactory and oxygen may be used alone when blood pressure is low.

RECONSTRUCTION OF THUMB*

A NEW TECHNIC

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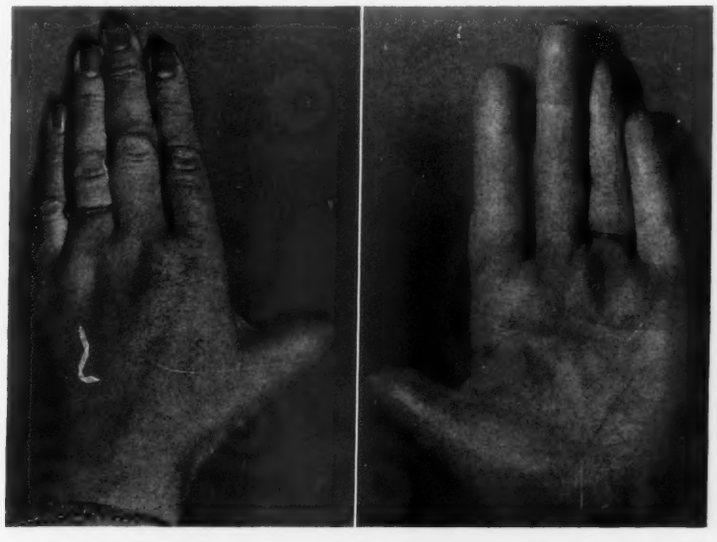
THE hand is the most important part of the upper extremity and the thumb is the most important part of the hand. Loss of a thumb means not only disfigurement but what is more important, the loss of the usual and proper function of the hand. Thus the thumb is vital from a functional and psychological viewpoint and becomes even more so when our hands are important to us economically in industry or in professional life.

For example, the case herein illustrated is a woman of fifty-one who, as a result of an industrial accident, lost part of her thumb. This meant loss of livelihood since her skill as a milliner went with the loss of the digit. To rehabilitate her thumb was therefore important to her and her family.

CASE REPORT

The deformity was produced in an accident while at work in a hat company when she stuck her left thumb with a milliner's needle. The digit became so badly infected that she was confined to a hospital for two months. When she was discharged she had a marked deformity of the left thumb. The nail, the distal phalanx and part of the proximal phalanx was missing. The tip of the remaining part of the thumb was covered with a firm scar that was very sensitive to touch. This meant that the patient could not use her thumb; the function of her hand was greatly impaired. (Fig. 1.)



A B

FIG. 1. A, loss of upper part of thumb (dorsal view). B, loss of upper part of thumb (palmar view).

To increase the size of the thumb to normal proportions and thereby restore the natural function of the hand a plastic reconstructive repair was indicated. Not only was a tubed

* Presented at the Symposium on Reconstructive Plastic Surgery at the West Side Hospital and Dispensary, January, 1942.

pedicle graft of skin needed to restore the length of the thumb but a peg of bone was necessary to replace the lost phalanx. This

Fig. 2. Shows tubed pedicle of skin from abdomen attached to thumb.

meant that a series of procedures were necessary. They were as follows:

Under general anesthesia a tubed pedicle skin graft about the circumference of her normal thumb was prepared from the integument of her abdomen in the region of the left lower quadrant. The skin was rolled into a tube

A B

Fig. 3. Distal phalanx absent. Small part of distal portion of proximal phalanx has been amputated; soft tissue of thumb wider than normal.

by means of interrupted sutures of fine silk, but both ends of this tube were left attached to the abdomen. However, the wound under the tube was closed by undermining the opposing edges of the wound and approximating them with interrupted sutures of medium silk. The wound and tube were dressed with gauze saturated with azochloramid. The dressings were changed every other day and within a week to ten days the stitches were removed.

Three weeks after the tube had been formed

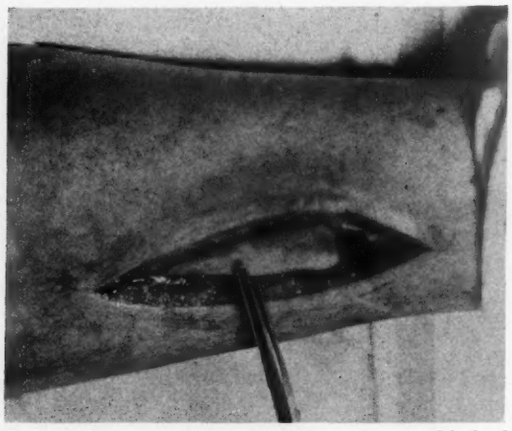


Fig. 4. Bone graft procured from lower third of left tibia.

the second stage of the operation was performed. Under general anesthesia the scarred area over the tip of the thumb was excised and the pointed extremity of the proximal phalanx was chipped off and rounded out. The distal end of the tube was then detached from the abdominal wall; it was subsequently unrolled to ensconce the tip of the thumb, that is the tube was attached to the raw surface of the thumb by means of interrupted sutures of silk. A plaster of paris cast was applied around the abdomen and arm to prevent motion of the graft, but an open window was left in the cast to permit view and treatment of the thumb and graft.

After two and a half weeks the cast was removed. The proximal end of the tube was detached from the abdominal wall and repaired in such a way as to simulate the end of a thumb. (Fig. 2.) The abdominal wound was closed by undermining and approximation of the wound edges.

Healing took place without any untoward result, but since the patient did not feel well she decided to wait a while before submitting to the other stages of the operation. However, during the next two months, her general condition was improved by medical and dietary treatment. At the end of that time radiographic examination of the left thumb showed the following (Fig. 3):

The distal phalanx was absent and a small part of the distal portion of the proximal phalanx had been amputated. The bony mar-

Fig. 5.

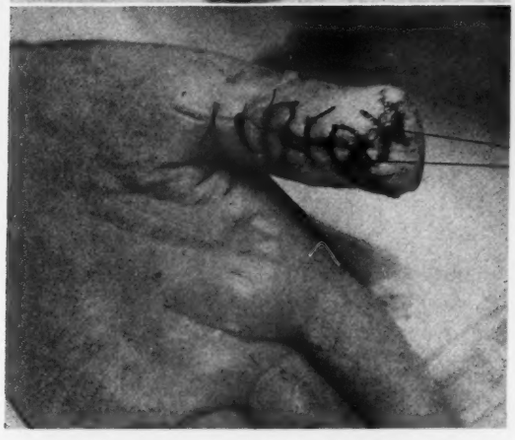
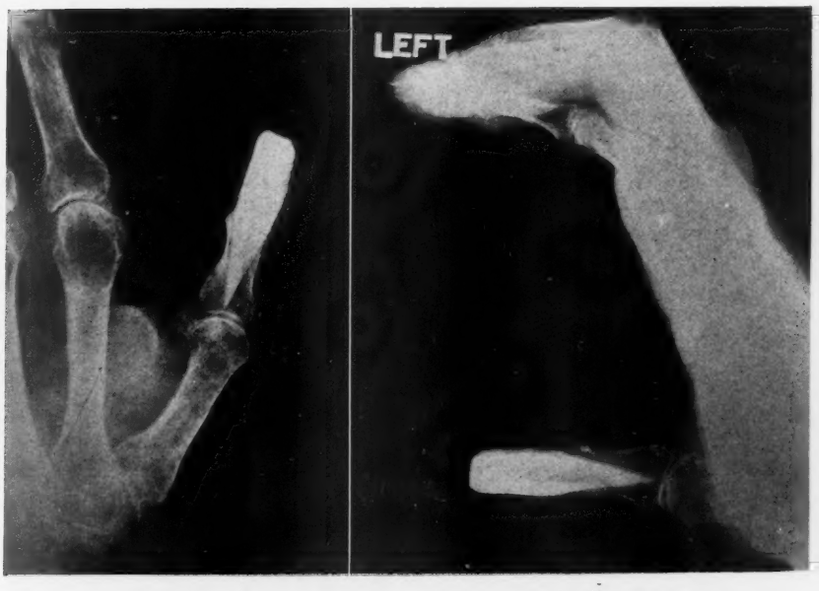


Fig. 6.

Fig. 5. Shows distal end of bone graft. Proximal end of this bone graft is wedged into the split proximal phalanx of thumb.

Fig. 6. Tube closed with interrupted sutures of silk.



A B

Fig. 7. Bone graft in perfect position wedged into proximal phalanx.

gins were smooth and there was no evidence of any gross pathological condition. The soft tissues of the thumb were wider than normal and had an artificial character which showed no indication of the presence of disease.

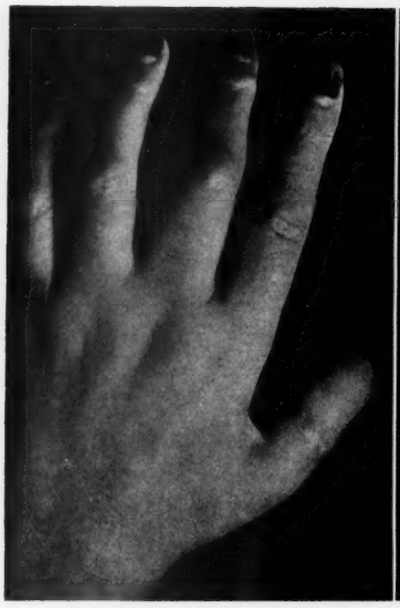


Fig. 8. Tip of thumb rounded out to simulate natural appearance.

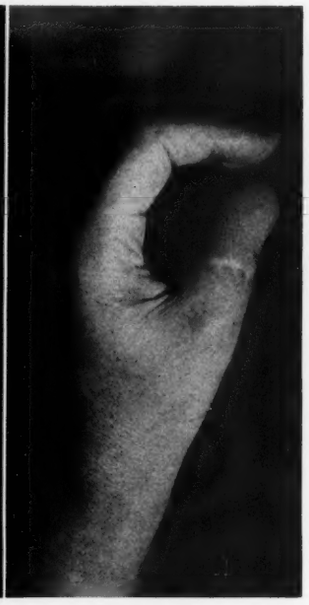


Fig. 9. Function of thumb restored; ability to adduct thumb to fingers indicated.

Finally she submitted to the next procedure. This consisted in a bone graft operation. I was assisted at that time by Dr. R. Preston. The soft tissues of the skin flap were opened to expose the proximal phalanx of the thumb. This phalanx was split longitudinally with the Albee motor saw, the saw cut extending from the distal end to about one-fourth of an inch from the proximal end of the phalanx.

From the lower third of the left tibia (Fig. 4) a bone graft about 2½ inches long was removed with the Albee saw. The proximal end of this bone graft was shaped as a wedge. This wedge was of the proper length and shape to fit into the previously split phalanx of the thumb. (Fig. 5.) The distal end of the bone graft was about ⅝ of an inch wide. This portion of the graft extended a distance of about 1½ inches beyond the end of the split phalanx.

The soft tissues of the flap and stump of the thumb around this graft were closed with interrupted sutures of No. 0 chromic catgut and the skin was closed with interrupted sutures of medium silk. (Fig. 6.)

A plaster of paris cast then immobilized the stump of the thumb and the graft; this cast extended to about the upper third of the forearm. The cast remained in place for about eight weeks and when removed, radiographic examination (Fig. 7) revealed that the bone graft was in perfect position, wedged into the proximal phalanx.

Two weeks later, a plastic operation was done on the integument and subcutaneous tissue of the tip of the thumb to give it more natural shape. (Fig. 8.)

Figure 9 shows proper closure of fingers of hand and ability of the thumb to adduct to the fingers. Of course, the joint between the proximal and distal phalanx is gone but the usual and important function of the thumb has been restored. Figure 10 shows the palmar view. The thumb looks perfectly normal but minus a nail. Figure 11 shows palmar view of thumb with artificial nail. Figure 12 shows dorsal view of artificial nail and thumb. The thumb is adducted to the fingers showing restoration of function.

For the purpose of quick easy undermining of the skin I have perfected a double-edged detachable knife. (Fig. 13.) The value of the double-edged feature is obvious in that the knife is twice as sharp as the ordinary one and, therefore, can be used

twice as long and twice as effectively without change of instrument.

At the rearward portion of this double-edged blade is a v groove designed to abut the walls in the projection of the handle member. There is an orientation knob on the handle which informs the surgeon which sharp edge he is using. The part of the blade that is not sharp is rib-backed which permits easy detachment of blade from handle.

The idea of a detachable blade is not new, but the double-edged feature is original and exceedingly useful not only in plastic repair but in any form of surgery as well.

It is gratifying to learn that Dr. A. H. McIndoe, head of the plastic reconstructive division of the R. A. F. is at present using this knife on wounded pilots with excellent results.

Fig. 10. Palmar view; nail missing.

Fig. 11. Palmar view; artificial nail attached.

Fig. 12. Dorsal view showing artificial nail attached; ability to adduct thumb to fingers indicated; normal function of thumb restored.

Fig. 13. Author's double-edged detachable knife.

CONCLUSION

I believe that this type of procedure is the most advantageous for the reconstruction of not only the thumb but of other fingers as well. It proves that the knowledge of bone grafting as practiced by the orthopedic surgeon can come in good stead for the reparative surgeon in order to achieve excellent functional and cosmetic results in such cases.

PLACENTA ACCRETA FOUND AT CESAREAN SECTION FOR PLACENTA PREVIA*

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PLACENTA accreta may be defined as that pathological entity in which the placenta is intimately adherent to the musculature of the uterus, due to a deficient or absent decidua basalis. This condition was known to the older obstetricians who called it adherent placenta. Berry Hart, in 1899, and Huffmeyer,[1] in 1890, were the first to publish observations of this condition which included histological studies.

Placenta accreta is a rare obstetric complication. In 1938, King[3] reported three cases of his own and stated that the total number of cases in the literature was 109 at that time. The frequency of occurrence varies from one in 40,000 cases as stated by Hirst[4] to one in 20,000 cases reported by Kraul;[5] one in 12,000 by Kraften;[6] one in 8,000 by Stoeckel[7] and one in a little under 2,000 reported by Irving.[8] An average incidence from the figures of ten observers is one in 14,600 deliveries.

Placenta accreta has been found as early as the third month of gestation and occurs up to full term pregnancy. Normally, the placenta is made up of villi and intervillous spaces and the decidua basalis is found beneath the villi and is penetrated by them in some places. In other words, the decidua basalis lies between the villi and the myometrium. The decidua basalis is made up of two layers, the compacta which lies near the villi, and the spongiosa which lies against the myometrium. After expulsion of the fetus the venous spaces are filled with blood and with the contractions and relaxations of the musculature separation occurs between the compacta and the spongiosa, at a plane where the erosive process of the trophoblast in the decidua stops. The slightly grayish, firmly adherent membrane which one normally sees on the maternal surface of the recently delivered placenta is the decidua compacta. When the decidua spongiosa is absent separation is difficult. When the decidua compacta is completely or partially absent, the separation is even more difficult. If the chorionic villi are in direct contact with the muscle layer, separation is impossible without tearing portions of the myometrium. When the decidua compacta is thin or absent, we speak of it as placenta accreta vera. When the villi penetrate into the muscle, we call the condition placenta increta. There may be partial or complete placenta accreta. In other words, only a part or the entire placenta may be firmly attached to the uterus. (Figs. 1 and 2.)

We must differentiate placenta accreta from adherent placenta. The big differential point is that in adherent placenta a plane of cleavage between the placenta and the uterine wall exists and is readily found. This is not so in placenta accreta.

The causes of placenta accreta may be summarized as follows: Repeated and vigorous curettage; manual removal of the placenta with one or more previous pregnancies, with resultant damage to the endometrium; submucous fibroids with atrophy of the overlying mucosa; endometritis as in a preceding postpartum infection; faulty position of the placenta as in placenta previa; pregnancy in a diverticulum of the uterus, for example, bicornuate uterus in which the endometrium may be

* Read at the Beth David Clinical Society Meeting, February 9, 1942.

poorly developed; previous cesarean section. The placenta may imbed itself at the site of the scar in the uterus at which point there may be a poor decidual reaction. In patients with functional disturbances and sterility the administration of hormones or synthetic drugs having hormonal-like effects may cause changes in the endometrium, which would perhaps be a factor in an altered decidual reaction and thus contribute toward the development of placenta accreta.

The literature consists almost entirely of case reports. In 1933, Pfaneuf[9] grouped eighty-two collected cases under four headings of treatment: (1) Manual extraction; (2) vaginal hysterectomy; (3) abdominal hysterectomy, and (4) cesarean section.

The maternal mortality figures for these four methods of treatment are as follows:

No. of Cases	Method of Treatment	Maternal Mortality, Per Cent
36	Manual extraction	72
11	Vaginal hysterectomy	36
33	Abdominal hysterectomy	6—Method of choice
2	Cesarean section	0

In one of these cases a hysterectomy was done; the other patient was treated by intrauterine packing; both mothers recovered.

In a survey of the literature I have found only the two above mentioned cases of placenta accreta in which a cesarean section had been performed for placenta previa. The following is a report of a third case which may belong to that group called placenta previa cervicalis by DeLee. In this type of placenta previa the placenta grows down into the cervical canal where a poor and unsatisfactory decidual response takes place with resulting invasion of the trophoblast into the cervical tissue and abnormal mechanism of separation as described above for placenta accreta. As no placental tissue was palpated in the cervical canal in this case, the diagnosis of placenta previa cervicalis is only presumptive in this instance.

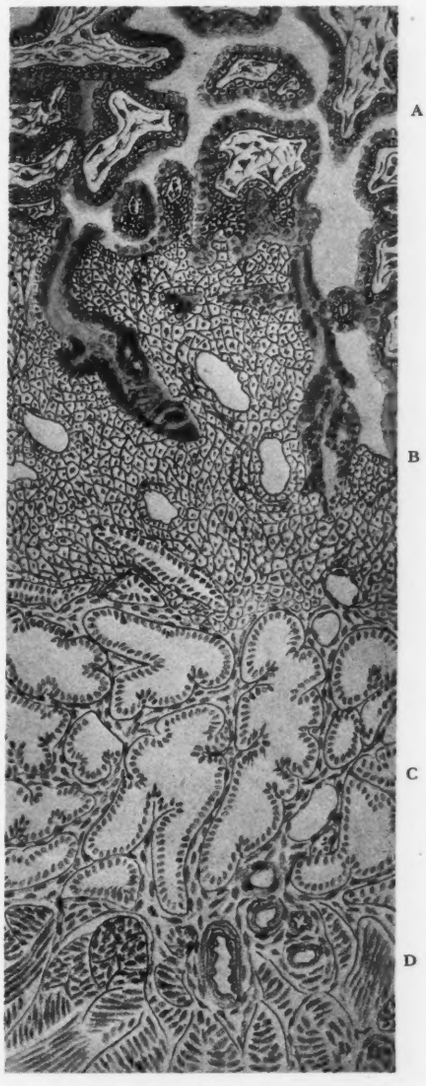

Fig. 1. Normal placental site. A, villi and intervillous spaces; B, decidua compacta; C, decidua spongiosa; D, myometrium.

CASE REPORT

Mrs. McA., thirty-eight years old, was admitted to the Beth David Hospital December 11, 1941. The past history is important. Ten years ago, September 23, 1931, she had a high forceps delivery with a second degree laceration, and a postpartum hemorrhage. The infant weighed nine and one-half pounds and died on the third neonatal day. The patient ran a febrile postpartum course and developed a pleural effusion of the left chest. She eventually

was discharged from the hospital, but had to be taken home by ambulance. Since that time she had one (early) pregnancy five years ago, which

Fig. 2. Placenta accreta. A, villi and intervillous spaces; B, one small area of decidua compacta; C, villi in direct contact with myometrium. (From Novak's Gynecological and Obstetrical Pathology, page 464. Philadelphia, 1940. W. B. Saunders.)

was terminated upon the advice of her physician because of her generally poor health; and three years ago she had a spontaneous five months miscarriage.

This patient was first seen by me September, 1941, at which time she was about five months pregnant. She had some slight painless vaginal staining for which she was treated by rest in bed and sedation. About three weeks later this painless bleeding recurred. A vaginal examination at this time revealed a cervix with an external os of two fingers. No placenta could be felt. She was about then six months pregnant. A provisional diagnosis of placenta previa was made and usual conservative therapy was followed. She was quite well for about six weeks when a third episode of painless bleeding occurred. Upon getting out of bed one morning she passed about four ounces of blood. The patient was then referred to Beth David Hospital.

A soft tissue *x*-ray taken shortly after admission was diagnosed placenta previa. She was kept in bed in the hospital for three weeks, during which time she spotted a little occasionally. The reason for this temporization with a diagnosis of placenta previa was that the fetus appeared small and its viability was questionable and this thirty-eight year old woman was very anxious for a living baby. The patient was typed and a donor for a blood transfusion was secured. Under observation during these three weeks the gravid uterus became much larger and the fetus appeared distinctly viable. On January 2, 1942, when she was about thirty-seven weeks pregnant, the patient began to bleed again, passing about four ounces of blood. It was decided that she had been carried long enough with a diagnosis of placenta previa, and now with a good sized viable baby there was no reason for delaying operation; therefore, she was delivered by cesarean section that day.

Under local anesthesia a transcervical section was performed, and a living female infant weighing seven pounds two ounces delivered. The transverse incision in the lower uterine segment came right down upon the placenta, thus proving the diagnosis of placenta previa. After the delivery of the baby and upon attempting to remove the placenta I found that a part of it was firmly attached to the lower uterine segment in the region of the cervical os. Most of the placenta which lay under the uterine incision was removed with two or three pieces having to be torn away from the site of attachment. The uterus was packed with plain gauze and the operation completed in the usual manner. The patient was given an infusion and transfusion of 600 cc. of blood following operation. She was kept in the operating room. Her condition was fair, her pulse was rapid and she was watched for vaginal bleeding. About one hour after the operation some vaginal bleeding was noticed. Although not excessive it was important to control this in a patient who had lost some blood during the operation. The patient was then placed in the lithotomy posi-

tion and a vaginal speculum was inserted. The cervix was exposed and grasped with sponge sticks. Digital examination at this time revealed another piece of placenta about the size of a walnut lying over toward the right side of the cervix. This was grasped with another sponge stick and had to be torn away from its site of attachment. There was moderately free bleeding following this removal. The cervix and vagina were then tightly packed with iodoform gauze. The patient was watched in the operating room for another hour until the bleeding was apparently controlled.

Postoperatively there was a fairly sharp febrile reaction as expected. The patient's pulse remained rather rapid for two days. The vaginal packing was removed at the end of forty-eight hours and the intra-uterine packing after seventy-two hours. After the initial febrile reaction she ran a low grade fever which finally reached normal on the nineteenth day. This was due to an endometritis which cleared rapidly with simple bed rest and small doses of sulfathiazole. She was discharged on the twenty-third postoperative day in good condition.

DISCUSSION

Hysterectomy was considered at the time of operation. I decided against the procedure because most of the placenta had been removed and only several small pieces remained in the region of the cervix. Hysterectomy would have meant total abdominal hysterectomy, that is, the uterus and cervix would have had to be removed because the parts of the placenta remaining were in the cervix and not in the body of the uterus. A supracervical hysterectomy would, therefore, have been a useless procedure and a total abdominal hysterectomy of a postpartum uterus at this time would have been too much surgery for this patient. In addition, the bleeding at the placental site was apparently controlled by the intra-uterine packing which remained dry during the closure of the uterus.

CONCLUSION

1. A case of placenta accreta in placenta previa treated by cesarean section is described.

2. The common causes of placenta accreta are mentioned.

3. Placenta accreta should be considered in any patient giving a history of repeated curettages or previous endometrial infection.

4. As a result of the increased number of cesarean sections placenta previa will probably become more common.

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MASSIVE RESECTION OF SMALL INTESTINE

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THE following is the history of a patient on which a massive resection of the small intestine for a volvulus was performed. This patient was operated upon at the age of nine years. She survived the operation and during the past five and half years she has developed normally.

CASE REPORT

Case No. 1249. W. S. D., aged nine years, a white, American, female child was admitted to the St. Francis Hospital, Peoria, Illinois, on September 21, 1936, under the care of Dr. C. E. Sibilsky, pediatrician. Her chief complaint was that of severe cramps in the abdomen. The following history was obtained from the child's mother: The child was a normal, full term delivery. Weight at birth was eight and three-fourths pounds. She was breast fed for one year. Even at this early date there was a tendency to constipation and glycerine suppositories and enemas were frequently required to give relief. She had the usual childhood diseases. She had suffered no injuries and no surgery was ever required. The family history was negative.

The child's present trouble began at the age of one year. This was attributed to the taking of more solid foods. After eating a meal one day she suddenly became stiff and pale, doubling up with colicky pain in the abdomen. Vomiting accompanied the attack. Similar attacks with cramping and vomiting had occurred periodically up to the present time. The attacks were more frequent during the early years of the child's life and she had as many as fifty attacks in a single year. In the past two or three years they had been decreasing in frequency and increasing in severity. The child had always been constipated and the mother stated that she believed her bowels were "paralyzed." Mineral oil and petrolagar had been given nightly for eight years.

The present attack of pain began on the afternoon of September 20, 1936. The onset was sudden and the patient complained of severe abdominal cramps in the region of the umbilicus. The pain was quite severe in character and the paroxysms became more and more frequent and were accompanied by vomiting. An enema gave only temporary relief.

I saw this patient on the afternoon of September 23, 1936. This was two days after her admission to the hospital and approximately three days since the beginning of the attack of pain. An *x*-ray (Fig. 1) was taken at St. Francis Hospital the morning before I saw her. The following is the report by the rontgenologist: "The heart and aorta within normal limits. The posterior mediastinum clear. The excursions of the diaphragm normal. The esophagus showed no pathology. The stomach was normal in size, shape, and position. There were no filling defects on either curvature. The pyloric antrum was regular in outline. The duodenal bulb presented no pathology. The stomach showed a definite retention at the end of six hours, about one-fourth of the original contents remaining therein. There was motility of the barium meal at the end of twenty-four hours. There was definite retardation at the end of twenty-four hours. There was definite retardation of the barium meal in as much as it was still located in the small bowel. There was some small bowel dilatation with an acute angulation in the right side at the level of the fourth lumbar vertebra, and an attempt at serrated edges of the small bowel which was quite suggestive of small bowel obstruction."

Physical examination revealed a poorly nourished child of nine years. Her expression was quite anxious and she looked much older than a child of her age. She was quite emaciated. Her thighs were flexed on her abdomen and she complained bitterly of cramp-like pain. When asked where the area of pain was, she pointed to the region of the umbilicus. The abdomen was soft and there was no rigidity. Tenderness was not marked on deep palpation. No masses were felt. Examination was otherwise negative.

The white cell count was 54,000 and the red cell count 3,500,000. Hemoglobin was 70 per cent. Differential count: segs ninety-one; staff one; young none; eosinophiles none; basophiles

none; lymphoblasts three; mononuclears five. Urine was negative; temperature 101°F. and pulse 130 to 140.

A diagnosis was made of bowel obstruction with peritonitis. An immediate operation was advised and the patient was prepared for surgery. Two hundred and fifty cc. of citrated blood was given preoperatively. No preoperative medication was given because of the patient's condition. The operation was performed under cyclopropane anesthesia and started at 4:45 P.M. On opening the abdomen through a right rectus incision, the cecum was found up under the diaphragm on the right side. There was a volvulus of the small intestine extending from the cecum to what seemed to be the upper portion of the ileum. The bowel was black and degenerated and there was definite evidence of the usual peritonitis with gangrenous bowel. It is roughly estimated that it was necessary to resect from ten to twelve feet of the small intestine. However, because the bowel was so badly degenerated, it was difficult to measure it correctly. At the lower portion of the ileum there was a large diverticulum which may or may not have been the original source of the trouble. No attempt was made to make anastomosis because of the patient's condition. The terminal portion of what was thought to be the jejunum and a small cecal portion of the ileum were exteriorized.

The patient required a very small amount of anesthesia. The operation was completed in thirty minutes. Her condition was poor throughout the operation and the prognosis was guarded. Her pulse ranged from 130 to 160. She was immediately given a transfusion of 250 cc. of citrated blood and the transfusion was followed by intravenous glucose and saline.

The next morning she was somewhat improved. Her pulse ranged from 120 to 140. She was given 300 cc. of citrated blood and also intravenous fluids. That afternoon she suddenly became cyanotic and her respirations increased to thirty-six. There was marked distention of the abdomen. An intranasal Levine tube was inserted. By aspiration and vomiting, approximately four to six liters of liquid were obtained and the patient had immediate relief. A Wangensteen suction tube was inserted. On September 25, the patient's general condition was a little improved. The return through the tube was only slightly colored. Her temperature was 102.8°F. Hemoglobin was 48 per cent and the white cell count was 8,800. Urine was negative. On September 26, she continued to show improvement. Intravenous fluids were given

FIG. 1. *X*-ray showing evidence of obstruction of small bowel before operation.

and the Wangensteen tube continued. The clamp which was left on the cecal portion of the ileum sloughed off. There was drainage from the upper loop. Her highest temperature was 101.8°F. Her hemoglobin was up to 63 per cent and the red cell count 3,370,000; the white cell count was 10,400. On September 28, there was no distention of the abdomen. The patient's highest temperature was 102°F. rectally. Her pulse ranged from 108 to 120. The cecal clamp was replaced. She was given sodium chloride by mouth. September 29, her general condition was good. She was given small amounts of fruit juice and jello by mouth. Her temperature was 99.6°F. On October 2, the patient was quite drowsy. Fluids were insufficient. There was a considerable amount of drainage from the jejunal loop. Fluids were given intravenously.

On October 4, a temporary artificial anastomosis of the loops by Y tubing was attempted but this proved unsatisfactory. The following day anastomosis by flanged glass tubing was done. There was passage of ileal contents into

the cecum for a brief period. The next day the cecal tube was removed and then re-inserted. Fluids were given intravenously and by mouth.

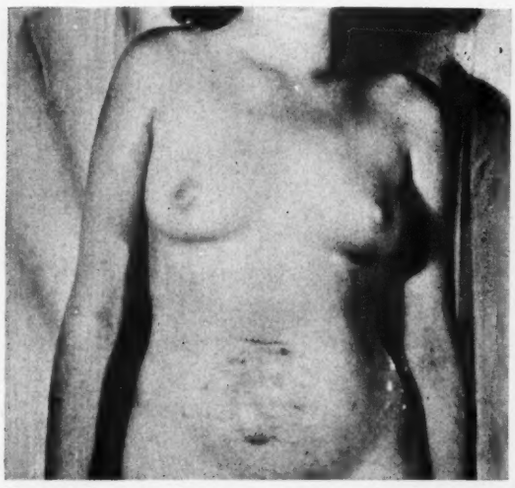

FIG. 2. Patient, five and a half years after operation, showing normal development.

There was still a large loss of ileal content from around the glass tube. There was obvious weight loss. On October 9, preparation was begun for anastomosis. Irrigation of the upper loop was done and a rubber dam was applied to protect the incision. On October 12, an ileocecal or questionable jejunal cecal end-to-side anastomosis with closure of the incision was done. The patient's general condition postoperatively was satisfactory. She was given 250 cc. of citrated blood postoperatively. Intravenous fluids were also given but nothing by mouth. On October 16, the patient's general condition was satisfactory. Intravenous fluids were continued. Her hemoglobin was 72 per cent and red cell count 3,540,000. Urine was negative. There was only a slight amount of drainage from the incision. She had several small liquid stools. On October 18, the patient was placed on a light soft diet. She had three to five stools in twenty-four hours. Her temperature was practically normal. On October 22, she had an occasional vomiting spell. She also had frequent loose stools. There was some separation of the incision. However, she seemed to be progressing satisfactorily. On October 28, the low fat, high protein, high carbohydrate diet with vitamins was increased. The patient's general condition was good. The stools were less frequent and more solid. On November 9, her condition continued good and she weighed forty-five pounds. She was able to be up in a wheel chair. She was discharged from the hospital on November 14, 1936, the wound being entirely healed except for two small areas. Her general condition was

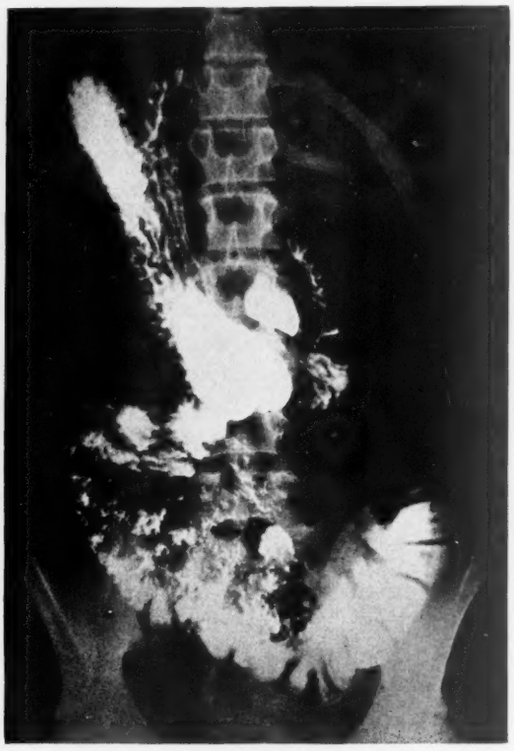

FIG. 3. *X*-ray of gastrointestinal tract five and a half years after operation.

good. She was advised to continue on the diet previously prescribed.

The patient made a good convalescence after her discharge from the hospital. She gained ten pounds in the first two months. I did not see her again until November 5, 1938, at which time she was getting along fine. She had gained a considerable amount of weight and her mother stated that she was better than she had ever been.

On September 22, 1941, five years after the operation, she came in for a check up at my request. Her appearance (Fig. 2) was that of a normal young lady. Her physical examination was negative except for a rather disfiguring scar on the abdomen. There was no evidence of a hernia. Her general health was good and she stated that she menstruates normally each month. She also stated that she had not been too careful about her diet. She does have two to three soft-to-liquid stools daily. She guards against taking laxatives.

A check *x*-ray of the gastrointestinal tract (Fig. 3) was taken at St. Francis Hospital. The

report of the rontgenologist is as follows: "Fluoroscopic examination of the chest negative. The esophagus was rather long and its distal end was close to the lesser curvature. The duodenal bulb was also close to the middle portion of the lesser curvature. The stomach emptied rather slowly but showed no defect. About two feet of the small intestine were visible. This portion of the intestine was normal in caliber and showed normal mucosal pattern.

"Films showed the configuration of the stomach as described above with no intrinsic defect. The duodenum followed the usual course. A moderate length of small intestine of normal pattern was visible in the middle portion of the abdomen. It was impossible to give an accurate statement of the length of the small bowel but it was judged to be near two feet in length. A film about fifteen minutes after barium was given showed only a small portion in the duodenum and proximal jejunum the remainder was in the stomach. At fifty minutes to one hour there was already barium in the cecum and ascending colon. The cecum was slightly more medial in position than usual. At two and one-half hours there was still a small amount of barium in the stomach and duodenum while the remainder was scattered throughout the small intestine and most of the colon. Hence, barium meal passed more rapidly through the intestine because of its short length but the motility of the various segments of gastrointestinal tract remaining was essentially normal for each individual area. The stomach was possibly a little slower to empty than the average."

Impression. Absence of most of small intestine (post-operatively); gastrointestinal tract otherwise negative.

Complete laboratory tests were also made. Blood chemistry: serum chlorides 643 mg. per cent; total proteins 7.25 per cent; albumen 5.4 per cent; globulin 1.85 per cent. Blood count: hemoglobin 72 per cent; red cell count 3,400,000; white cell count 5,800; color index 1.06. Differential count: segs fifty-three; staff three; young none, eosinophiles none; basophiles none; lymphoblasts forty; mononuclears four. Urinalysis was negative. Urinary calcium twenty-four hours—232 mg. Feces examined for fat showed 23 per cent fat.

SUMMARY

I realize that I would not be reporting this case if the patient had not survived the operation. I also realize that no conclusions should be drawn from one case. However, there are certain observations which might be noted.

The following observations have been noted in this case:

1. There was a definite advantage in making anastomosis to the cecum rather than to the transverse colon.

2. The child has seemingly developed perfectly normal through a rather critical period of her life and the only apparent residual effect which could be accounted for, on the basis of the amount of intestine removed, is the frequent loose stools and the mild secondary anemia.

3. The blood chemistry in this particular case is normal five and a half years after the operation.

4. Although an accurate measurement of the bowel removed was not made, I believe that the estimate of ten to twelve feet is quite conservative. An attempt to verify this was made by recent *x*-ray.

For an extensive and very comprehensive review of a collection of cases of massive resection, you are referred to an article by Dr. H. E. Haymond.[1]

The author wishes to express his appreciation to Dr. R. I. Clary, former associate, and to Dr. C. E. Sibilsky, who referred the case, for their assistance in the postoperative care of the patient.

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HEMORRHAGIC SOFT TISSUE SARCOMAS*

REPORT OF TWO UNUSUAL CASES

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TWO tumors with unusual characteristics are reported, both occurring in the upper extremity. These are of clinicopathological interest because of their obvious soft tissue origin, their similarity in their tendency to extreme hemorrhagic necrosis such as is seldom seen except in telangiectatic osteogenic sarcoma (malignant bone aneurysm), their obvious possibilities of extensive fluid-like spread along fascial planes, and the fact that their outstanding characteristic was their resemblance clinically, and in one instance anatomically, to a large hematoma. On sectioning, the tumors were literally extruded in a gush of fluid blood leaving large cavities lined with fibrin and with but few areas of tumor cells. In one instance the normal tissues surrounding the fluid mass stood out as though exposed by anatomic dissection (Fig. 1) and the residual cavities, when further exposed, appeared to be filled with fluid, largely hemolyzed blood with some small clots in the dependent portions. In both cases extensive intratumoral hemorrhage had contributed to marked anemia.

CASE REPORTS

CASE 1. A seventy-two year old colored male, a native of the Virgin Islands, and by occupation a sugar planter, was admitted to the Memorial Hospital on September 15, 1937, with his chief complaint a swelling of the arm. There had been no previous serious illnesses. The family history was irrelevant. In December, 1936, the patient noted a painless, soft, fluctuant swelling of the right forearm. He was afebrile and the swelling did not interfere with function. The forearm gradually increased in size and by March, 1937, the swelling seemed to be pointing and almost ready to rupture. It was then incised by the family physician at its most fluctuant point, obviously under an erroneous diagnosis of abscess. There was a profuse discharge of blood, serum and slough.

Four months later the patient consulted a second physician. At this time he was in a critical condition because of the continuous oozing of blood and because of secondary infection. A submitted report of the physical examination made July 2, 1937, is as follows: "Patient is a short, thick, obese man of about 70 years of age, pallid, weak, and afebrile. There is a fusiform swelling of the right forearm. The wrist and elbow joints are not involved. There is slight edema about the wrist, but no swelling of the dorsum of the hand. There is no loss of function of the fingers. The arm above the elbow shows some edema. The skin of the forearm is smooth and soft. There are no nodules or points of tenderness. There is no local heat. From two holes in the skin oozes a serosanguinopurulent discharge. The margins of the openings show very hypertrophic, soft, sloughing, friable tissue. Digital examination of the cavity shows it to extend the length of the ulna. The surface of the bone is roughened. There appears to be no invasion of the skin. Roentgen examination shows a layer of new bone along the entire shaft of the ulna, and also along a part of the radius. There is no erosion of the cortex and the medulla appears normal throughout. Incontinence of bladder and rectal sphincters has been present for 45 days. Laboratory: Kahn negative; RBC 1,300,000; WBC 9,100; urine negative. On July 14 the extremity was amputated through the middle third of the humerus. Convalescence was uneventful. Recurrence in the amputated stump was noted September 5, 1937. The patient was sent to the Memorial Hospital for further treatment."

Physical examination on September 15 showed a well developed, obese, seventy-two years old negro male who appeared chronically ill. Head, neck and lungs were negative. Heart: A loud systolic murmur was heard over the aortic area. The abdomen was obese, genitalia atrophic, reflexes hyperactive, lymph-nodes not

* From the Pathology Laboratories, Memorial Hospital, New York City.

enlarged. *Local lesion:* The right arm had been amputated about the midshaft of the humerus; the wound was well healed. The skin of the stump was shiny, tense, edematous and reddened, with dilated superficial veins. Fluctuation was present over the lower portion. There was induration extending well up into the axilla and over the head of the humerus. There were no palpable axillary lymph-nodes. Roentgen examinations of the lungs and shoulder were negative for pulmonary metastases or primary bone tumor. *Laboratory findings:* red blood cells 2,528,000; white blood cells 9,200; urine showed a trace of albumen and many pus cells.

FIG. 1. Amputated upper arm of patient in Case 1. The tumor cavity has been opened through a longitudinal incision. Note blood vessels and nerves in the center of the cavity as though carefully dissected. The cavity is free of tumor other than the cells adherent to and growing in the wall. A section of the humerus has been removed, exposing the medullary cavity.

Treatment. The patient was given a preoperative course of *x*-ray therapy. Between September 16 and 24, through an anterior port measuring 21 by 10.3 and a posterior port 15.6 by 17.8, he received 400 R times 4 (factors, 200 kilovolts, ½ mm. cu. filter, 50 cm. TSD). One port was treated daily. Under ether anesthesia, an interscapulothoracic amputation was performed on September 29. A transfusion of 500 cc. citrated blood was given before and again immediately following the operation. Convalescence was uneventful.

Pathology. On admission, the patient presented for study the entire specimen of his previously amputated arm fixed in formalin. Examination of this specimen showed an upper extremity amputated through the midhumerus. There was a through-and-through incision of the skin, apparently made with the idea of evacuating pus. Dissection of the forearm showed muscles intact, connective tissue edematous, and here and there, over a wide area, some soft, friable, brick-red material resembling formalin-precipitated blood. This material had no definite anatomic relation to nerve, muscle or bone, and no bursae were identified as sites of origin. The material in one area extended down through periosteum and was continuous with bare bone. Throughout almost the entire length of the ulna, the bone cortex was thickened, elevated and irregular, like a callus in old osteomyelitis. The medullary cavity was small in diameter; the marrow was hyperplastic. An additional tumor apparently removed from the amputated extremity was received separately and looked like a mass of fixed blood clot.

Examination of the specimen removed on September 29 was of an interscapulothoracic amputation of the stump of the arm. There had been a previous amputation a little below the midhumeral region, 20 cm. of the humerus remaining. The stump was well healed. The arm was enormously edematous, tense and fluctuant. On sectioning, the entire length of the humerus from the point of amputation to the glenoid was surrounded by a cavity containing at least one liter of fluid blood, only the lower dependent portion being clotted. The hemorrhage had separated nerves and vessels as if by anatomic dissection. Numerous pockets of hemorrhage were traceable through muscle planes, and over part of the humerus the periosteum was exposed and roughened, as in the bones of the forearm previously described. Smears made from the fluid showed numerous

tumor cells. In the axilla there was some soft hemorrhagic tissue, which seemed to lie within the axillary fat and was certainly metastatic

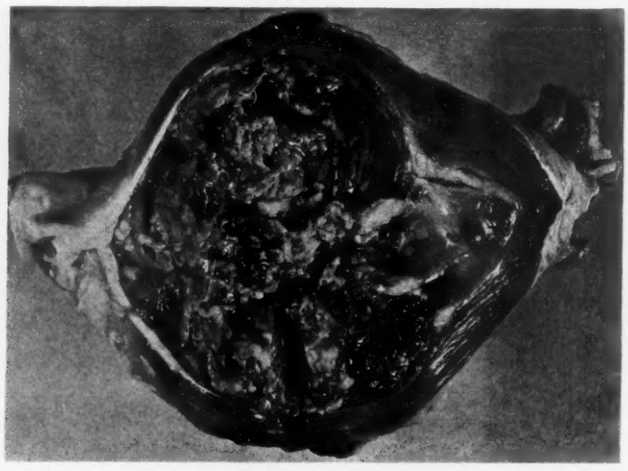

Fig. 2. Arm of patient in Case II opened by a longitudinal incision through the biceps muscle. Note the large cystic cavity, the wall of which is covered with necrotic tissue, fibrin, blood and tumor cells.

disease. There were some soft pinkish lymph-nodes, uninvolved by tumor.

Local recurrence was noted beneath the skin flaps in January, 1938. The patient, however, continued in good health until June, from which time onward he expectorated blood and became progressively worse. The local recurrence, too, became fluctuant. He died at home September 4, 1938, twenty months after the clinical onset of his disease. No autopsy was obtained.

Case II. A forty-eight year old Russian housewife was admitted to the Memorial Hospital with a chief complaint of tumor of the left arm. The family history was negative. Past history described a supravaginal hysterectomy, presumably for fibromyoma, three years before the present admission.

Nine weeks before admission a friend grasped her left arm and she experienced considerable immediate pain. Prior to this she had noticed no tenderness or swelling. Immediately following this alleged injury, the arm became swollen and painful. She consulted her family physician who prescribed diathermy and infra-red treatments three times a week for three weeks. The swelling and pain became more marked and she was hospitalized in another hospital where an exploratory operation was performed. The tumor encountered was described as being in such a degenerated condition that it could not be removed. She was given two deep *x*-ray therapy treatments over the arm and then referred to this institution. She had lost five pounds in weight; she denied any cough, hemoptysis or other complaints.

Physical examination revealed the patient to be a well developed, moderately obese, apprehensive, white female about forty-seven years of age. Head, neck, lungs, heart and breasts were not remarkable. The abdomen showed a well healed scar. The cervix uteri was soft and boggy; no fundus was palpable. There were no enlarged lymph-nodes. Reflexes were normal. *Local lesion:* In the region of the left biceps there was a large, irregular, firm, slightly tender mass involving the anterior half of the arm. The mass extended from the cubital fossa to the axillary fold and measured approximately 10 by 16 cm. There was a linear scar over the center of the mass. In the scar were two ulcerated areas, measuring 2½ cm. in diameter, from which oozed a small amount of purulent discharge. The mass was movable over the underlying humerus. There was definite skin attachment. The circumference of the left arm, 10 cm. above the condyle, measured 35 cm.; the right measured 29 cm. There was some limitation of motion of the left shoulder due to pain. There did not appear to be involvement about the shoulder joint; axillary, supraclavicular and cervical lymph-nodes were not enlarged. Roentgen examinations of the chest and humerus were negative for pulmonary metastases and bone involvement. Laboratory findings: red blood cells 2,848,000; white blood cells 8,200; urine negative.

Clinical Course and Treatment. On August 17, 1938, an interscapulothoracic amputation of the left upper extremity was performed. The

patient received a transfusion at the time of operation and again on August 20. Convalescence was slow but otherwise uneventful. On December 19, 1938, she complained of pain over the tuberosity of the right ischium. Local, pelvic and rectal examinations as well as roentgen studies of the pelvis and femur were negative. On January 16, 1939, there was a palpable tender mass in the right buttock. Aspiration biopsy of this mass was positive for malignant tumor. She received eight deep *x*-ray therapy treatments of 200 R each (factors, 200 kilovolts, ½ mm. cu, filter, 50 cm. TSD) through a port 13 by 13 cm. centered over the mass. The pain and the mass in the buttock disappeared. On March 10, 1939, there were extensive metastases to the lungs and the left femur. The patient died at home April, 1939. No autopsy was obtained.

Pathology. The specimen was a left upper extremity, including a portion of the clavicle and the entire scapula with the scapular muscles attached. Situated on the anterior lateral aspect of the arm, opposite the biceps muscle was a raised tumor mass. There was an old incision directly over the mass and in the scar was an ulcerated area 4 cm. in length. The skin was thin and ecchymotic and the tumor mass felt soft and fluctuant, suggesting a diffuse hematoma.

In the axilla were six or more lymph-nodes, the largest of which measured 2 cm. in diameter and on gross section appeared suspicious of metastatic tumor, although subsequent study showed it free of disease. Section of the tumor revealed no attachment to bone. It was almost completely confined to the belly of the biceps muscle and measured 15 by 8½ by 6 cm. The tumor was sectioned in a longitudinal direction and found to consist of a cystic cavity filled with old blood clot and degenerate, necrotic tissue. (Fig. 2.) There was no evidence of perforation posteriorly. There was some evidence of infiltration distally along the fascial planes toward the biceps tendon.

In neither of these cases may a histogenetic diagnosis of the nature of the tumors be rendered with certainty. Both tumors are clearly primary lesions. That of the second patient evidently arose in the belly of the biceps muscle and is in all probability a myosarcoma, although there is little confirmatory evidence to be derived from sections on account of the extreme hemorrhagic necrosis. Although this hemorrhagic liquefaction was grossly more extensive in the tumor of the first patient, nevertheless, somewhat more intact tumor was available for histologic study. In this instance the tumor may perhaps best be described by stating that it resembled a highly malignant telangiectatic osteogenic sarcoma in spite of its evident soft part origin. Large blood spaces were lined with hyperchromatic tumor cells with enormous single and multiple nuclei and with abundant acidophilic cytoplasm often filled with droplets, masses of red blood cells and hematogenous pigment. In better preserved areas, the growth appeared to be in the form of syncytial masses of rather uniform, medium-sized cells interspersed with tumor giant cells. Epulis-type giant cells, rare in the first case, were exceedingly numerous in the second and such cells again add to the tumor's resemblance to telangiectatic osteogenic sarcoma. In the tumor of the first patient were areas where erythropoiesis seemed to be occurring. The first tumor is classed provisionally as fascial sarcoma; the second as myosarcoma.

SUMMARY

1. Two extremely hemorrhagic soft tissue sarcomas* of the upper extremity are reported, one tentatively classified as fascial, the other as myogenic sarcoma.

2. These are of interest because of their clinical resemblance to hematoma due to their extensive hemorrhagic necrosis, the marked extent of fluid invasion in one instance along fascial planes, and the marked anemia caused by these tumors.

3. Their microscopic structure simulated, in properly preserved areas, telangiectatic osteogenic sarcoma, despite their obvious soft tissue origin.

4. The extreme hemorrhagic liquefaction, especially in the first case and particularly the degree of anemia presented by both patients suggest the presence of hemolytic properties resident in the tumors, since neither tumor revealed evidence of infection sufficient to explain the picture.

* Case 1 is presented through the courtesy of Dr. Bradley L. Coley. Case 11 is from the service of Dr. George T. Pack.

FISH BONE PERFORATION OF THE JEJUNUM*

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FISH is an almost universal food, and fish bones are undoubtedly ingested rather frequently. The number of swallowed fish bones, and the proportion of these that cause perforation or penetration of the bowel is obviously impossible to determine. Reports of such perforations of the gastrointestinal tract are relatively uncommon. The earliest recorded instance that has come to our attention was in 1841.[1] and we have been able to find only forty-three recorded instances since that time. Carp[2] collected forty-eight cases of swallowed foreign bodies from the New York Presbyterian Hospital files from 1915 to 1926. Of these, two perforated the gastrointestinal tract, one fish bone and one chicken bone. With the exception of a group of six cases described by Ginsburg and Beller,[3] these reports have been almost entirely of isolated instances.

Of the forty-three instances of perforations by fish bones, the stomach was involved in three, the small bowel in twelve, the colon in ten and the rectum in eleven. Two perforated a Meckels' diverticulum, two the appendix and in three the site of perforation is not reported.

Several reasons are advanced for this relative infrequency of perforations. Many bones are caught in the pharynx and not swallowed. Of those that are swallowed the majority are probably well surrounded by intestinal content and rendered harmless. Smaller bones may be digested, or at least softened, and rendered unable to perforate the bowel wall.

A bone that becomes lodged in the bowel mucosa may penetrate through the intestinal wall either by direct trauma or by pressure necrosis. The inflammatory process set up by pressure necrosis may aid in digestion of the bone. This process probably occurred in the case which we are reporting. In this instance the process led to an abscess of the bowel wall and perforation as well, but it seems possible that at times the bone may be sloughed back into the lumen of the bowel and further penetration prevented.

CASE REPORT

B. K., a twenty-five year old married woman was admitted to the surgical ward with a history of generalized abdominal pain for five hours. The pain had gradually increased in severity especially in the right lower quadrant. There was no history of dietary indiscretion, no nausea or vomiting. There was a past history of occasional right lower quadrant pain, which had been diagnosed as a "chronic appendix." The rest of the history was not pertinent.

Physical examination revealed a well developed and nourished woman obviously in pain, with a temperature of 100.2°F. rectally, a pulse of 92, and respirations of 22. The significant physical findings were limited to the abdomen. It was resistant to palpation, particularly on the right side. Tenderness was diffuse and marked. Rebound tenderness was exquisite over the right lower quadrant. No masses were palpated. Pelvic examination revealed nothing abnormal. There were 24,000 leucocytes per cu. mm. of blood. Urinalysis and examination of vaginal smears revealed nothing abnormal.

The preoperative diagnosis was acute appendicitis and the abdomen was explored through a muscle splitting incision. When the peritoneal cavity was opened, a moderate amount of cloudy fluid was encountered. The peritoneal surfaces were injected, as was the appendix. Exploration revealed an indurated area, 3 mm. in diameter, in the distal jejunum. This grey green area was the site of a pin point-sized free perforation of the bowel wall. It was completely excised and the defect sutured. The appendix was removed and the abdomen was closed without drainage. The patient left the hospital on the eighth postoperative day after an uneventful convalescence.

* From the Department of Surgery, Michael Reese Hospital, Chicago.

Questioning of the patient during her hospital stay revealed that two weeks before admission the patient ate fish. A bone lodged in her throat and it took about an hour to dislodge it by swallowing, eating bread crust, etc.

Fig. 1. Showing fragment of bone within localized abscess in wall of jejunum.

Pathologic report of the excised tissue was "Recent abscess in the wall of the small intestine with a fragment of bone in the wall. Acute perijejunitis." (Fig. 1.)

This case is interesting for several reasons. It illustrates the well known fact that bones may perforate the bowel wall by pressure necrosis and infection as well as by direct trauma. The finding of the bone fragment within the bowel wall indicates that bone destruction may occur as a result of the inflammatory reaction and digestive processes.

The necrosis and infection lead either to a free perforation as in this instance, or to a more gradual penetration with walling off of the involved loop of bowel by other intra-abdominal structures, which leads eventually to all the bizarre clinical pictures and symptomatology which have been recorded in the literature. It is easily understood why the time element varies so greatly between ingestion of bone and the start of symptoms. The various clinical types of perforations have been classified by Ginsburg and Beller:[3] (1) Acute perforation with peritonitis; (2) localized intra-abdominal abscess; (3) intra-abdominal inflammatory tumor; (4) abdominal wall inflammatory tumor; (5) abdominal wall abscess; (6) perforation with inflammation and obstruction in the hernial sac. The reason for occurrence of these groups is evident.

SUMMARY

1. The case report illustrates free perforation of the ileum by a fragment of fish bone not large enough to be recognized grossly.

2. Pressure necrosis and infection of the bowel wall by a bone or foreign body is well illustrated.

3. The possibility that most perforations occur through this process is suggested.

4. The possibility that digestion of the bone by the inflammatory process initiated may in itself be a mechanism to prevent perforation of the bowel wall by loosening the bone and sloughing it back into the bowel lumen is advanced.

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EXTERNAL PERFORATION OF THE ESOPHAGUS*

CASE REPORT

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WHILE internal perforations of the esophagus are relatively common, perforations from without are rare. This is due to the deep seated position of the esophagus, its rather small diameter in the resting, collapsed state and to the protection of the surrounding structures, particularly the spinal column. Because of their rarity these cases always present a problem in treatment since any one man's experience is usually too meager to form a basis for the proper management when a case presents itself. The primary consideration in these wounds is the control of the infection which develops in the lacerated area, to prevent mediastinitis or to treat it if it develops.

Jensen,[1] who reviewed four cases collected from the literature[2–5] and added one of his own, attributed the good result obtained in his case to an operation exposing the lacerated esophagus and inserting a drain, thus establishing, he believed, more adequate drainage; although he cites three cases which healed without operative intervention.

CASE REPORT

A white female, aged seven years, was admitted to the Milwaukee County Emergency Hospital on July 28, 1941. She had been running on a fence with a stick in her hand and had fallen, the stick perforating her neck. The stick was immediately removed with very little hemorrhage.

Examination revealed her to be very apprehensive. Her respirations were short and jerky. Her skin was pallorous. There was a laceration 2 cm. long just lateral to the sternal attachment of the left sternocleidomastoid muscle through which blood-tinged saliva oozed when she swallowed. Immediately surrounding the laceration there was an area of subcutaneous emphysema for a radius of about 2 inches.

The abdomen was tender throughout and held rather rigidly. The pulse rate was 110 and the quality was good. The temperature was 100°F., rectally.

A prophylactic dose of combined gas gangrene and tetanus antitoxin was given. A stomach tube was passed through the nose into the stomach. A hot compress was placed over the wound. Sulfathiazole, 1 Gm. three times daily, was administered; the tablets being crushed and placed into the tube feeding.

Five hours after admission, the temperature was 102°F. and remained at about that level throughout the entire next week. There was no undue pain or tenderness in the neck and the abdominal distress rapidly disappeared. The next morning the blood count was: white blood cells 12,700 and red blood cells 3,940,000. The emphysema showed no tendency to spread.

It was found advisable to divide the tube feedings into very small amounts and to give them every hour as too large quantities of fluid given at one time caused vomiting, some of the vomitus escaping through the neck wound.

After forty-eight hours the wound began to discharge pus mixed with saliva. A lateral *x*-ray of the neck revealed no abnormalities except the emphysema. The *x*-ray report on the chest was as follows: "There is a broadening of the mediastinal shadow, especially to the right with haziness in the inner lung field on this side. There is some interstitial emphysema of the left side of the neck. Impression: early mediastinitis."

Repeated chest *x*-rays on August 4th showed some increase in the cloudiness of the mediastinal shadow. (Fig. 1.) The patient, however,

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exhibited none of the clinical signs or symptoms of mediastinitis except the elevation in temperature which was not of the septic type. Because

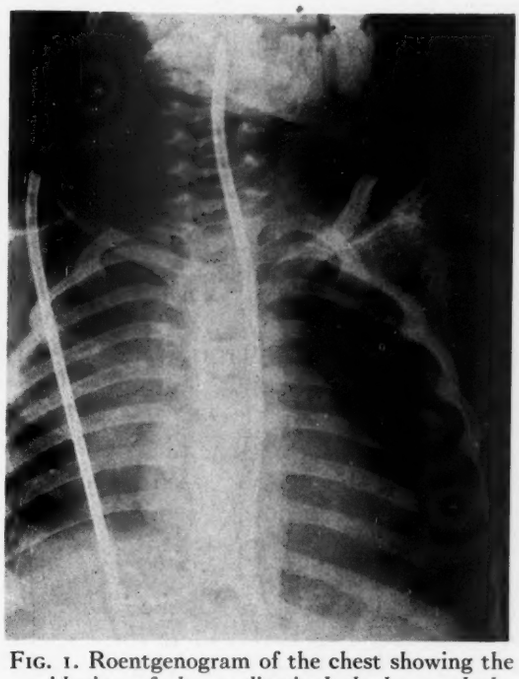

Fig. 1. Roentgenogram of the chest showing the widening of the mediastinal shadow and the haziness in the right inner lung field. The two white streaks show the stomach tube in the esophagus and externally from the nose.

of the patient's lack of symptoms it was believed that, if a mediastinitis was present, the wound itself afforded adequate drainage and that the chemotherapy was preventing a fulminating mediastinitis.

On August 5th, the emphysema was gone and the temperature returned to normal. On August 7th, fluids were given by mouth as the fistula was closed and August 9th, twelve days after the injury, the stomach tube was removed. Figure 2 shows the patient after the wound had healed. On September 1st, a fluroscopy of the esophagus using barium sulfate showed no abnormality and the mediastinal shadow was normal.

DISCUSSION

The emphysema occurring immediately after the accident as in this case should not alarm one, since it is due, as Holinger[6] states, to the aspirating effect of the negative intrathoracic pressure during inspiration.

It was believed that there was nothing to gain by operative interference. To attempt to repair the esophagus would have meant a fairly extensive neck dissection with more resultant trauma to tissue and with a

Fig. 2. Three weeks after the injury. The healed neck wound is indicated by the arrow.

possible pocketing off of infection. As far as the treatment of the infection was concerned, it was believed that the injury had performed a perfect cervical mediastinotomy with very adequate drainage. We are of the opinion that the chemotherapy aided in preventing a fulminating mediastinitis.

SUMMARY

A case of external esophageal perforation treated conservatively is reported with a brief review of the literature.

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COCCYGEAL HERNIA

CASE REPORT

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COCCYGEAL hernia is a rare type of postoperative hernia; it is not mentioned in textbooks of surgery even among the rare hernias. This hernia does not occur congenitally and there is no case on record in which a hernia has occurred in this region where there has not been performed a previous operation for removal of the coccyx. In reviewing the literature I was able to find only two other cases reported.

CASE REPORT

The patient, a white married woman, aged twenty-eight, was admitted to the Birmingham Baptist Hospital on August 3, 1939. She injured her coccyx in March, 1937, and following this injury she had considerable pain in the coccygeal region. Five months after this injury her coccyx was removed in another hospital following which she had an infection of the sutures but no general breaking down of the wound. After recovery from this operation she was free from symptoms for approximately twenty months; then the structures gradually broke down and on April 1, 1939, she first noticed a protrusion in the region of the coccyx. Three weeks after the protrusion occurred she began to have a dull pain in this region when sitting or standing. She always had good control of her bowels and no constipation had been present. She had one child which was six years old; her menstrual periods had been normal. The family history was irrelevant.

She was well developed and well nourished. The systolic blood pressure was 115, the diastolic blood pressure was 75, the pulse rate was 90, and the respiratory rate was 20. The rest of the examination revealed that there were no abnormal findings except in the coccygeal region where a well healed scar was present in the midline. When the patient was sitting or standing there was also present in this region an oval protruding mass 5 to 6 cm. in diameter. (Fig. 1.) This mass was soft, easily reducible end on coughing a definite impulse could be alicited. When the patient was put in the recumbent position the mass entirely disappeared.

The laboratory report showed that the urinalysis was negative. The hemoglobin was 78 per cent, the red blood count was 4,000,000 and the white blood count was 9,000 with 72 per cent neutrophiles and 28 per cent lymphocytes.

A diagnosis of coccygeal hernia was made and on August 4, she was operated upon by Dr. Earle Drennen. The operation was done under spinal anesthesia with the patient in the prone position.

She was dismissed from the hospital on August 9, and was to continue rest in bed at home. Her convalescence was uneventful except for a small amount of serous discharge from the wound. One year after the operation the patient was in good condition and had no recurrence of the hernia or the symptoms.

Pagenstecher reported a case of coccygeal hernia in 1930, and Nichols and Herring reported a case in 1933. Of these three cases reported (including the case reported here) two were females and one was a male. (Table 1.) The age of these patients was fifty, thirty-eight and twenty-eight, respectively. In each case there had been done a coccygectomy previously. In the first case the time between the removal of the coccyx and the occurrence of the hernia was seven months, in the second case it was seven years, and in the third case it was twenty months. The duration of the hernia in the first case was four months, in the second case six weeks, and in the third case four months. Two of the cases had pain in the coccygeal region especially when sitting, but one case complained of only the sensation of the protrusion of her bowels and the sensation of sitting on her bowels.

In the second case the hernia started after a subsequent injury to the coccygeal region following the removal of the coccyx. The anal sphincter was functioning properly in all three cases, for no incontinence was present in any case. There was no strangulation of the hernia present in any case. The final result following the repair of the hernia was good in all three cases with no recurrence of the hernia up to the time of the last observation.

TABLE I

OUTLINE OF CLINICAL FINDINGS IN CASES OF COCCYGEAL HERNIA

Author	Age	Sex	Symptoms	Length of Time between Removal of the Coccyx and the Occurrence of the Hernia	Condition of the Wound Following Removal of the Coccyx	Duration of Hernia	Final Result
1. Pagenstecher....	50	Female	Presence of the sensation of protrusion of the bowels and the sensation of sitting on the bowels	7 mos.	Drainage for 3 mos.	Less than 4 mos.	No recurrence after 9 mos.
2. Nichols and Herring.	38	Male	Dull aching pain in lower end of spine especially when sitting	7 yrs.	Drainage for few days but healing by first intension	6 wks.	No recurrence after 3 mos.
3. The Author.....	28	Female	Dull pain in coccygeal region when sitting or standing	20 mos.	Infection of the sutures	4 mos.	No recurrence after a year

The anatomic structures in this region are very strong and dense and it is not probable that a hernia would occur here spontaneously unless it followed the surgical removal of the coccyx or severe traumatic laceration of this region.

The etiology of coccygeal hernia is essentially the same as that of postoperative hernia in the anterior abdominal wall. Infection and the improper approximation of the important muscles and fascia are the chief causes. In each of the three cases studied here there were signs of some wound infection. In the first case there was drainage of the wound for a period of three months. In the second case there was drainage of the wound for a number of days, but the wound healed by primary intention. The third case according to the history had an infection of the sutures. If the attachment of the muscles and fascia is stripped from the lower end of the sacrum during the removal of the coccyx, that would greatly increase the tendency for the formation of a hernia.

ANATOMY

The coccyx which has the attachment of many important structures forms an essential link in the supporting mechanism of the posterior pelvic wall. Beneath the skin and the two layers of superficial fascia the main structures are the glutei maximus muscles with their covering sheath, the fascia lata. These are attached to the sides of the coccyx, lower part of the sacrum, and the sacrotuberous ligaments. Anteriorly to the origin of the gluteus maximus on the coccyx the sacrotuberous and sacrospinous ligaments are attached, and in front of these ligaments is the point of insertion of the coccygeus muscle which helps to close the posterior part of the pelvic outlet.

Of the structures which help to support the anal diaphragm the coccyx gives insertion on its anterior surface to the levator ani muscles; the two pubococcygei muscles unite forming a fibromuscular band which lies on the raphe of the iliococcygei muscles. Superficially to the levator ani muscles the apex of the coccyx gives attachment to the anococcygeal raphe which extends from the tip of the coccyx to the posterior margin

of the anus and gives attachment to the circular fibers of the sphincter ani externus. Closely associated with the levator ani muscles is the pelvic fascia.

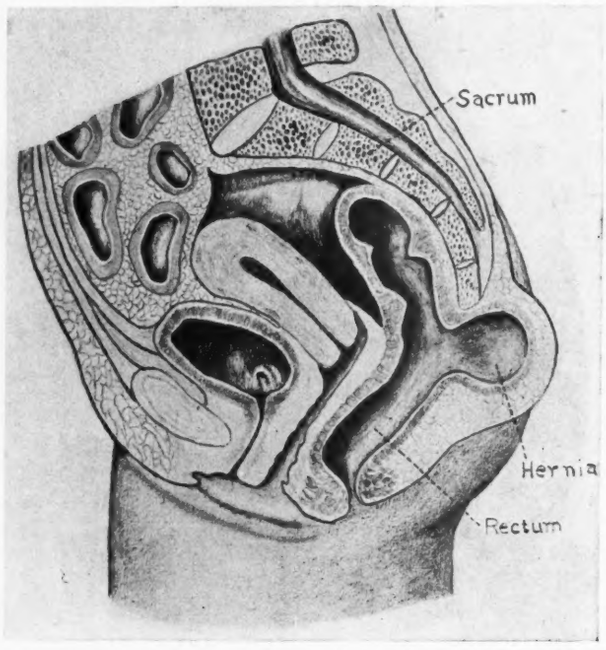

FIG. 1. Drawing of a median sagittal section illustrating a coccygeal hernia. The coccyx is absent and bowel is protruding through the coccygeal region.

A hernia in this region protrudes through the triangular area which was occupied previously by the coccyx. It is bounded above by the lower end of the sacrum and on each side by the gluteus maximus muscle. The apex of the triangle extends into the levator ani muscles. Externally, it is covered by skin and superficial fascia.

OPERATIVE PROCEDURE

The patient is put in the prone position and a midline incision is made in the skin directly over the mass. Upon extending this incision down through the subcutaneous tissue the posterior surface of the bowel is brought into view. There usually is no peritoneal sac present, for the posterior surface of the ampulla of the rectum which is not covered by peritoneum forms the protruding mass. If no peritoneal sac is present, the protruding mass may be inverted by simple plication. The posterior part of the levator ani muscles is freed and any separation that has occurred in them is sutured. The gluteus maximus muscle with its fascia and sacrotuberous ligament are freed on each side and these structures are firmly sutured in the midline. In the lower end of this suture line some of the sutures are so placed as to include the levator ani muscles and thus help to support the anal diaphragm. The superficial fascia and skin are closed in layers.

CONCLUSIONS

A case of coccygeal hernia is reported and two other cases are reviewed from the literature. The following conclusions are drawn from a study of these three cases:

1. Coccygeal hernia is an incisional hernia which occurs only following the surgical removal of the coccyx or severe traumatic laceration of the coccygeal region.

2. A postoperative wound infection is a definite etiologic factor in the formation of this hernia.

3. The length of time between the removal of the coccyx and the occurrence of the hernia has been from seven months to seven years.

4. A hernioplasty done by the dissection of the important anatomic structures and their approximation in layers gives a good result.

I want to express my gratitude to Dr. Earle Drennen for granting me permission to publish his private case.

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New Instruments

REFRIGERATION BOX FOR AMPUTATION*

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ICE anesthesia for amputation of extremities is now being regarded as a very satisfactory procedure for the debilitated, toxic and poor risk patient. Crossman and Allen have a convincing series of amputations performed under ice anesthesia in which the absence of shock is a notable feature. We have had a similar experience in a smaller series of cases. One case in particular illustrates the effectiveness of ice anesthesia in decreasing the shock of operation as well as the shock of anesthesia in sick, debilitated, aged individuals.

CASE REPORT

N. B., sixty-seven years of age, was admitted to Dr. Fredrick W. Bancroft's service at the Beth David Hospital on July 24, 1941, with the diagnosis of diabetic gangrene of the left foot and lymphangitis extending above the ankle. The patient ran a septic temperature during the entire preoperative period. The cardiac status was so poor that any mental excitement or sitting up in bed produced cyanosis and marked dyspnea. Aware of his bad cardiac state, a very brief inhalation anesthesia was given on two occasions, once for amputation of the toe and the other time for incision and drainage of the plantar fascia. On both occasions the patient went into acute cardiac failure with pulmonary edema. He required heroic treatment for his resuscitation. On September 29, 1941, one week after the incision and drainage, the patient was prepared for a midthigh amputation by refrigeration in our box. He not only withstood operative procedure without discomfort, pain or cardiac embarrassment but was able to get into a wheel chair the afternoon the day of operation for the first time in two months.

The method that we originally used to produce refrigeration was to place a rubber sheet under the affected extremity, pack ice around the leg and then enclose the whole in a rubber sheet. The melting ice wet through bed sheets and mattresses and offered a difficult nursing problem. The transportation of the patient with his leg wrapped in ice to the operating room was also inconvenient.

The box we have devised and used obviated these difficulties. The box is made of wood, is rectangular in shape and measures thirty-six inches in length, fifteen inches in width and fourteen inches in height. The lining is of galvanized tin. The bottom of the box is round and semicircular and accommodates two rockers, one near its proximal end and one near its distal end. The rounded bottom and rocker construction give the box a cradle-like motion enabling the patient to change his position in bed. The proximal rocker is four inches in height and the distal rocker is two inches in height. The difference in height of the two rockers produces an incline permitting easier drainage of the water from the melting ice. In the proximal end of the box there is a round opening measuring ten inches in diameter sufficiently large to accommodate the largest thigh. The upper section of the opening is made removable, enabling one to place the leg in the box without having to guide the foot and leg through the opening of the box.

* From the Surgical Service of Beth David Hospital, Dr. Frederick W. Bancroft, Surgical Director.

The removable piece is then replaced, thus completely encircling the thigh. The extremity is further sealed within the box by slipping a rubber inflatable ring over the leg and placing it flush against the opening. On the floor of the distal end of the box there are two outlet tubes permitting the drainage of water so that ice particles alone surround the leg. The box is covered by a lid which is fastened in place by two hooks on each side.

Fig. 1. Refrigeration box without cover. Removable upper section in proximal end of box is in place. This section is removed when extremity is placed in box. Outlet tubes for drainage are at distal end of box.

The technic we have employed consists first of placing three ice bags to the site at which the tourniquet is to be applied. These are left in place for fifteen minutes producing superficial anesthesia so that the application of the tourniquet may be painless. After the tourniquet is applied, the rubber inflatable ring is drawn over the leg proximal to the tourniquet and the entire extremity including the tourniquet and rubber ring is placed in the refrigeration box which has been filled about one-third with small pieces of ice. More ice is then placed in the box to cover the entire extremity. The lid is then fastened in place and the leg remains refrigerated for a period of two hours. The patient with the extremity enclosed in the box is then

Fig. 2. Extremity in place; upper section in place. Extremity in midthigh amputation would enter box to level of groin. Tourniquet around the limb not depicted; rockers on bottom of box not visualized. Galvanized tin lining within wooden box with rounded bottom can be noted.

transferred to the stretcher and brought to the operating room. The leg is removed from the box while being transferred from the stretcher to the operating table. The surgeon then proceeds with amputation, the tourniquet being removed prior to the closure of the wound in order to control hemostasis.

The operation, in our experience, has been painless and has not required any supplementary anesthesia. I believe this has been the experience of Dr. Crossman in his larger series of cases. Less preoperative medication is necessary than is used for general anesthesia. It is also necessary that the leg be defrigerated slowly after the amputation by the use of ice bags to the stump for two to three days.

THE important problem in the induction of anesthesia by inhalation is to establish and maintain a free airway so that the anesthetic agent can enter the lungs, pass from the lungs into the blood stream, and by the blood be carried to the nervous system. It is often important to employ some device which will prevent the tongue and epiglottis from obstructing the space above the larynx.

A NEW INSTRUMENT FOR USE IN BILIARY SURGERY

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THE retractor herewith illustrated was designed to give a maximum exposure of the biliary ducts with minimum effort on the part of the assistant. From the standpoint of the assistant, it is almost foolproof.

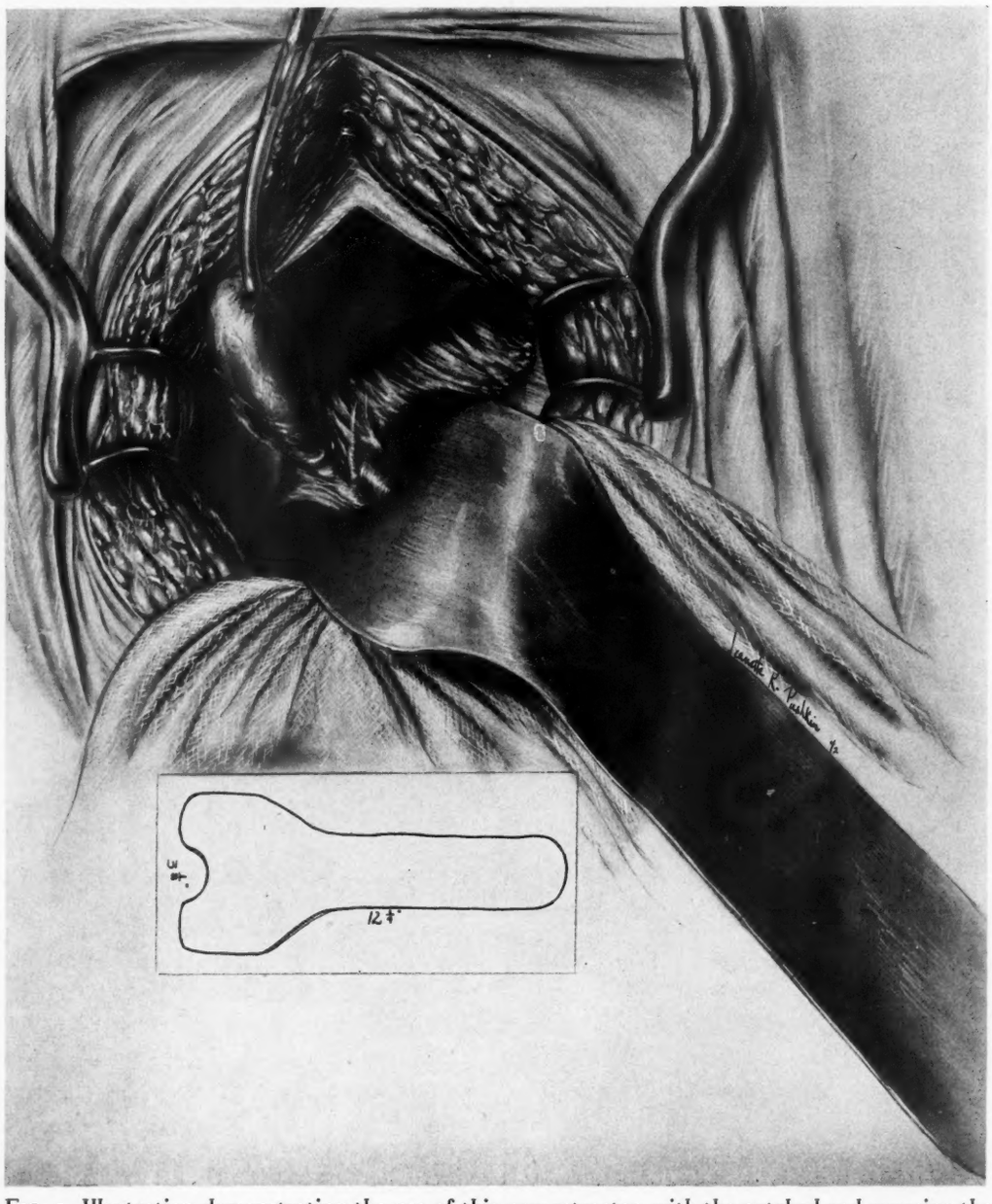

FIG. 1. Illustration demonstrating the use of this new retractor, with the notched end exposing the cystic and common bile ducts, portal vein and the hepatic artery.

* Dr. R. H. Walker passed away on February 19, 1942, a few days after the receipt of this manuscript.

Before developing this retractor, it was my practice to use the assistant's left hand for retraction in exposure of the ducts. The hand took up considerable space and was constantly shifting. In addition, the left forearm and shoulder of the assistant were frequently in the way of the operator. These annoyances were removed by this specially designed instrument.

The retractor is made of the same material as the so-called "ribbon retractors." It is, therefore, pliable and can be bent to adjust itself to any curve in securing exposure of the ducts. It is 12¼ inches in length, 3⅛ inches wide at its broadest end and 1¾ inches at the narrowest end. The broad end is notched so that the retractor may rest down over the ducts without injury to them, and at the same time secure the greatest possible amount of exposure.

Diagnostic block anesthesia usually is carried out for patients who complain of various disturbances, the most common of which is pain; it is also used when the pathway of the pain cannot be determined exactly, so that blocking of one or more pain pathways assists in establishment of the differential diagnosis.

The brief excerpts in this issue have been taken from "Clinical Anesthesia. A Manual of Clinical Anesthesiology" by John S. Lundy, W. B. Saunders Company.

NEW ATRAUMATIC NEEDLE FOR FASCIA SUTURES

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THE value of fascia sutures, either living or preserved, in the repair of hernias and in bridging defects of the abdominal wall, is well known. Unfortunately, however, there has been restriction of the use of fascia, and often abandonment, because of trauma produced in suturing. Large needles and unwieldy methods of attaching the fascia to the needle cause splitting and fraying of the tissues, and thus may seriously weaken and endanger the repair.

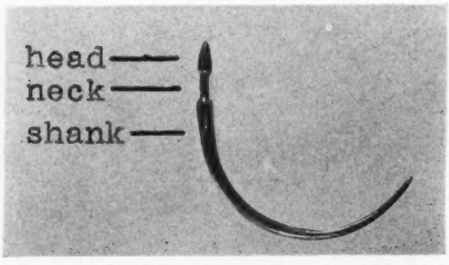

FIG. 1. Needle enlarged to show detail.

A new and atraumatic needle is presented here to simplify the use of fascia and to lessen trauma. The unique principle is best indicated by Figure 1.

The needle is round, full-curved and has a taper point. The greatest diameter is in the shank at the junction with the neck. The neck obviously is much smaller and the head is a slight enlargement at the end of the neck, just large enough to prevent the fascia from slipping off.

The fascia is placed on the neck, long axis of the strip in the long axis of the needle, with the end of the strip at the junction of the neck and shank. It is bound around the neck with six or seven turns of tightly wound fine silk thread. (Fig. 2.) It has been shown that great pull will not dislodge the fascia strip.

The advantages of this needle may be listed as follows: (1) Attachment of the fascia strip to the needle is accomplished simply and quickly. (2) The fascia suture can be easily drawn through tissues because the combined diameter of the neck and fascia is no greater than the largest diameter of the shank of the needle. Obstruction to passage by knotting of the fascial strip, as is necessary when eye type needles are used, is thus obviated. (3) This needle may be made considerably smaller than other needles used for this purpose because of the unique principle employed. (4) The entire length of the strip of fascia is conserved. No part of the length need be sacrificed to make a knot, as is the case when eye type needles are used; nor is there any loss because of fraying as may be the case with slot type needles. The silk thread binding the fascia to the neck is simply unwound or cut away to release the fascia from the needle.

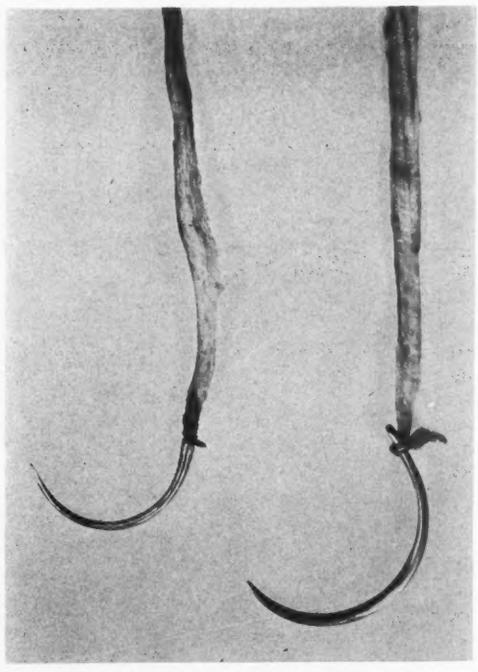

FIG. 2. Atraumatic and eye-type needles compared in size and mode of attachment of fascia strip.

METAL STIRRUP FOR KNEE SUPPORT IN APPLYING A PLASTER CAST

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As everyone applying plaster casts knows, support of the knee while putting on a hip spica is difficult. If a bandage or a rope is used, it hugs the limb, is incorporated in the plaster; and, if removed, it comes away with difficulty. Moreover, plaster bandages cannot be readily passed between the arms of the loop.

To obviate this difficulty, I have devised a square metal stirrup, the top and sides made of steel and the bottom of pipe. A ring at the top is for attaching a rope. The vertical arms are bent at a right angle to fit into the pipe. The leg, properly padded, rests on the bottom of the stirrup. Plaster bandages are easily passed through it. When the cast is firm, the arms are sprung from the pipe, which is now removed. The cast may be reinforced if necessary. One use of this stirrup will prove its value. It can be made by any mechanic.

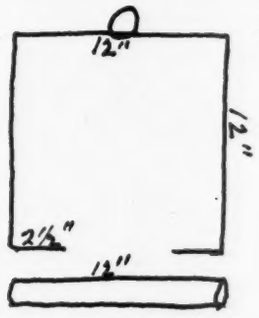

Fig. 1. Arms of the stirrup separated.

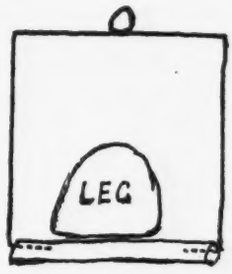

Fig. 2. Stirrup assembled; leg in position.

OPPONENS THUMB WIRE SPLINT

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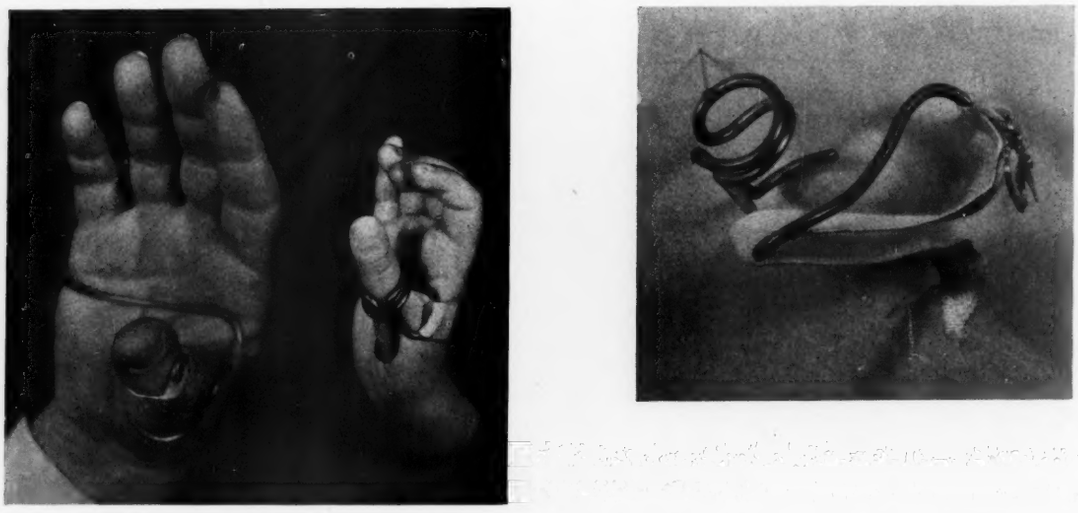
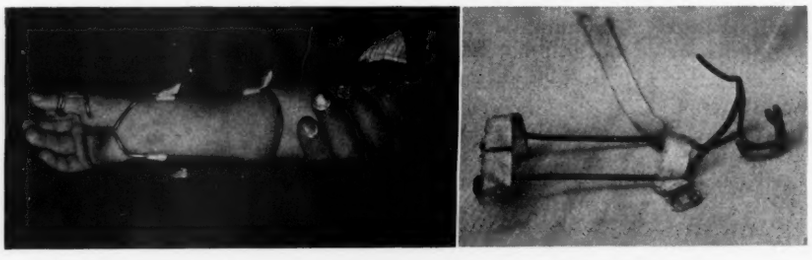
THE efficiency of this opponens thumb splint has surpassed, in my experience, that of other types of braces employed in an effort to hold the thumb in its functional position. It is extremely light in weight and is constructed, in each instance, from one continuous piece of clothes-hanger wire. The wire that fixes the thumb in opposition and partial abduction crosses the palm of the hand and terminates in an ulnar flange. In Figures 1A and 1B the brace is held by a strap across the dorsum of the hand and permits free wrist motion, while in Figures 2A and 2B the brace has been incorporated in a cock-up splint.



A B

FIG. 1. The opponens thumb wire splint as utilized in cases wherein free wrist motion is permissible. It has proved very efficient in the treatment of the flat hand, illustrated on the right of (A), of a child with residual paralysis following acute anterior poliomyelitis.



A B

FIG. 2. The combined opponens thumb and cock-up wrist splint, constructed from one continuous piece of cloths-hanger wire, as utilized on the hand and forearm of a child with spastic hemiplegia.

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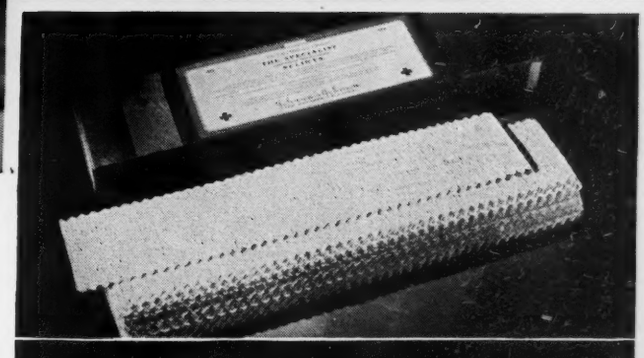

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*Hamilton, J. E., A Comparative Study of Local Burn Treatments, Amer. Jl. Surg.: Dec., 1942.

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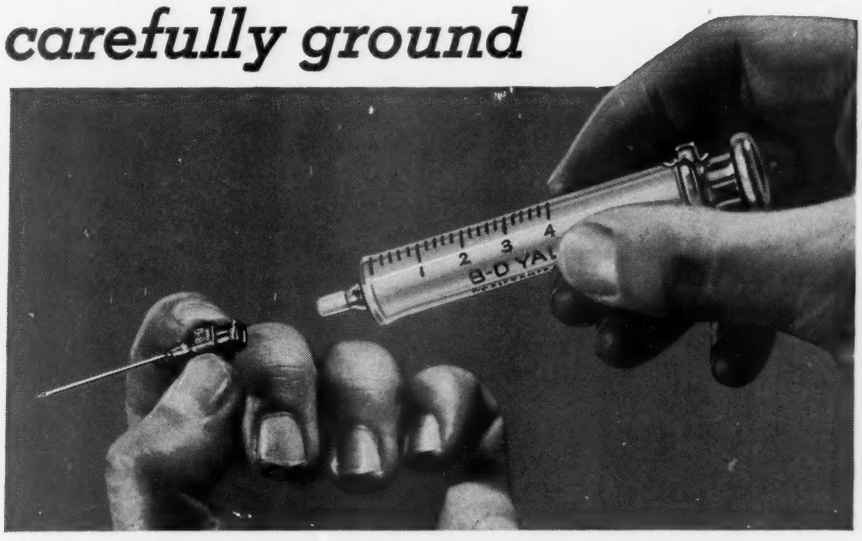

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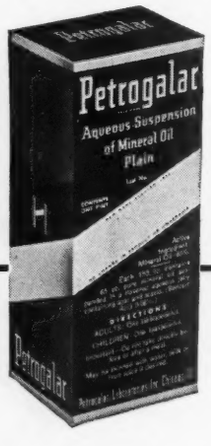

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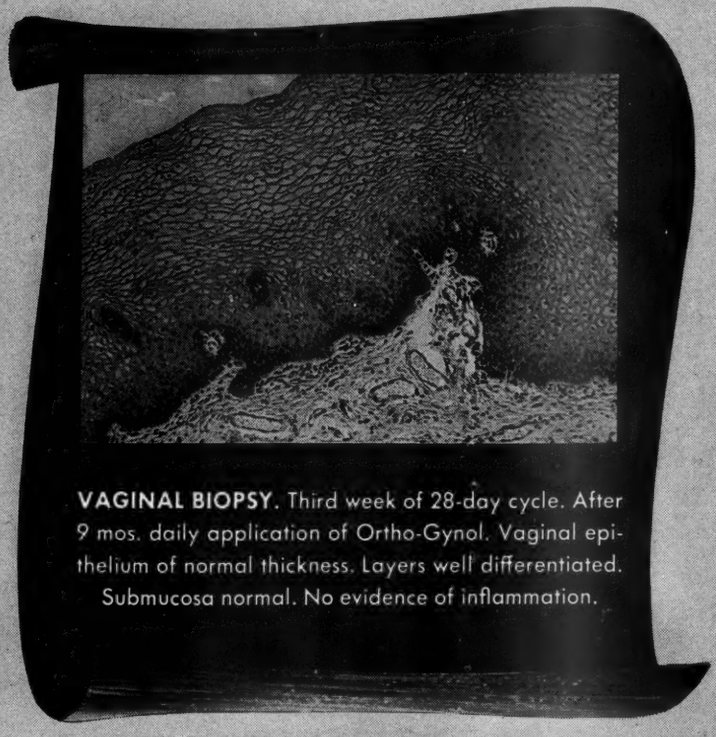

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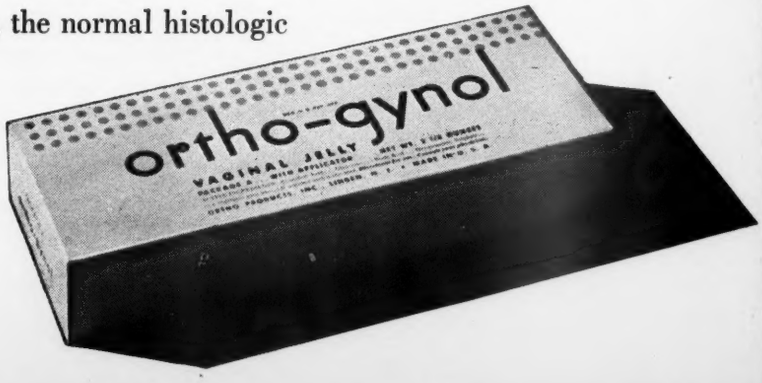

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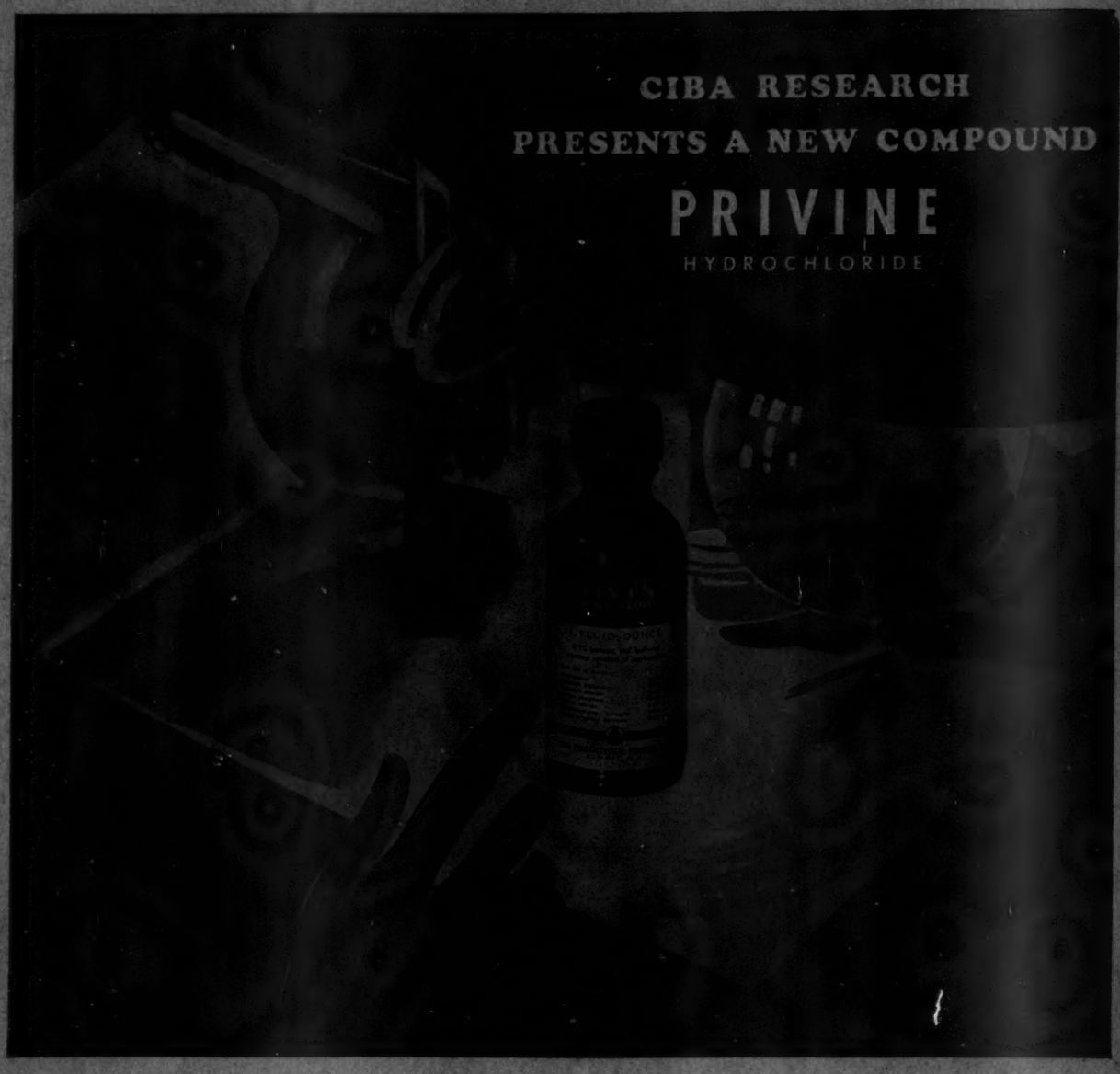

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